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Bulletin on NARCOTICS

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GENERAL

The Cultivation of the Opium Poppy in India

By S. N. Asthana, M.Sc.
District Opium Officer, Bareilly

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I. History of the opium trade in India

When and how the opium poppy and its produce became known to the people of India is uncertain. In the *ain-i-Akbari* compiled by Sheikh Abul Fazl, about A.D. 1590, the poppy is mentioned as a staple crop of the spring harvest of the then Subhas of Agra, Oudh and Allahabad. Up to the period of the British acquisition of Bengal and Behar, the Dutch were the chief purchasers of opium. Instructions to make opium a part of the investment were first issued by the East India Company in A.D. 1683.

The triumphs of Suraj-ud-Daula over the European Companies in 1756 brought ruin to the Patna opium dealers. On the restoration of peace in 1765, very little opium was to be had and the price went very high. In 1767 the Companies made a joint concern of the trade, with one general agent for all the opium produced, and finally in 1773 an end was put to all these disputes when the Governor of Bengal assumed on behalf of the East India Company, a monopoly of all the opium produced in Bengal, Behar and Orissa.

From 1773 to 1793 the right to the exclusive manufacture of opium for the Company was sold annually at first, but, from the year 1781, by four-year contracts.

In 1797, the agency system took the place of the contract system and the control of the Opium Department was vested in the Board of Trade, the President of which was practically an *ex officio* Member of the Council.

The opium monopoly was promulgated in India by the Opium Act of 1857 (Act No. XIII of 1857); the monopoly of manufactured drugs was established by the Opium Act of 1878 (I of 1878) and the Dangerous Drugs Act of 1930 (II of 1930).

After the transfer of power to the Government of India in 1947 and the promulgation of the Constitution of India in January 1950, the control over the cultivation and manufacture of opium throughout India passed into the hands of the Government of India on 1 April 1950. By virtue of the Opium and Revenue Laws (Extension of Application) Act, 1950, No. XXXIII of 1950, the three Central Government enactments, viz., the Opium Act of 1857, the Opium Act of 1878 and the Dangerous Drugs Act of 1930, now apply uniformly in all the States of the Indian Union.

A central authority, the All-India Narcotics Board, was established by Resolution No. F.235-E.0/45 of the Ministry of Finance (Revenue Division) of 2 April 1949, in order to improve and co-ordinate the various aspects of the narcotics administration throughout India. The Board is responsible to the Ministry of Finance and is assisted by a narcotics adviser and the necessary staff in the performance of its functions. In November 1950, the Government of India took the first step in a programme to unify and rationalize the system of control over the production of opium throughout the country by creating a central organization.

The Department is now controlled by the Narcotics Commissioner, Government of India. Cultivation is carried on on behalf of the Government by growers who undertake to sow the poppy, lance the capsules, collect the latex, and deliver the drug at the weighing centre at a price fixed by the Government of India. A traditional initial advance is given to the cultivators in Uttar Pradesh, at the time of sowing. The opium received from the cultivators is sent to the Government factories at Ghazipur or Neemuch, where it is chemically tested and prepared for export and internal consumption.

II. Geographical distribution in the world and in India

The plant is not indigenous to the country and was imported from abroad. *Papaver somniferum* is originally a native of the warmer parts of western Asia from where it was taken to Greece. From Asia Minor the Arabs traders took it to the Far Eastern countries, including India and China.

There can be little doubt that the medicinal poppy is a native of Western Asia but it is cultivated at the present time not only in the original area of distribution but also in India, Iran, Turkey and Europe.

P. somniferum is sometimes found apparently wild in Britain. It is now extensively cultivated in most of the States of Europe not on account of the opium as in India, Turkey, and Iran, but on account of the capsules and of the oil obtained from the seeds.

According to Duthie, the opium poppy, unknown as a wild plant, is now generally regarded as having originated through cultivation from a Mediterranean species. The truly wild plant (var. *Setigerum*) is found on the northern coast of the Mediterranean. It has toothed leaves, the lobes sharp-pointed, each ending in a bristle. The flower stalks and sepals are covered with scattered bristled hairs and the stigmata are seven or eight in number.

During the beginning of the Christian era opium and its properties were universally known. During those days, opium was chiefly produced in Asia Minor and its cultivation grew into a big industry.

P. somniferum has been extensively grown in India for its milky juice, which is obtained by scarifying the capsules when fully grown but in a green state. During the middle of the eighteenth century Behar was the chief province of India which produced the best quality and the greatest quantity of opium. At present, poppy cultivation is confined to the States of Uttar Pradesh, Madhya Bharat and Rajasthan and Himachal Pradesh, the present acreage area being one tenth of what it used to be four decades ago.

III. Species of *Papaver* and varieties of *P. somniferum*

The genus *Papaver* contains about 110 species with many varieties and forms, mostly natives of Central and South Europe and temperate Asia. Five species occur in Great Britain. *P. rhoeas* is the common scarlet poppy found in fields. Cultivated forms of this species, with exquisite shades of colour and without any blotch at the base of the petals, are known as Shirley poppies.

In India, the only wild poppy is *P. croceum*, which grows in the Alpine regions of the Himalayas along the borders of the glacial streams or near water at altitudes of 12,000 feet to 18,000 feet. The flowers are orange coloured. In this part of India the poppies are annual ruderals, usually growing in grain fields in the spring. Two species have prickly capsules. *P. hybridum* has rather small brick-red flowers and *P. pavonium* is much more hispid especially on pedicels and peduncles and has larger salmon or orange flowers with a dark centre. *P. pavonium* seems to be able to stand dry places better than *P. hybridum*. There are a few species also with smooth capsules.

P. dubium var. *glabrum* has orange or salmon flowers with a dark spot near the base of each petal. It is common in many parts of Northern Punjab. Like *P. pavonium* it also grows in the North West Frontier Province. *P. marcostonum*, *P. turbinatum* and *P. rhoeas* are common in the wheat fields of Kashmir.

The following are the three main varieties of *P. somniferum*:

1. *P. somniferum* var. *nigrum:* A wild form of the opium poppy with purple-red flowers, roundish oblong capsules, opening by pores under the stigma, with seeds of a dull greyish-black colour.

2. *P. somniferum* var. *album:* Also a wild form with white flowers, roundish ovate capsules, not opening by pores under the stigma. Seeds white.

3. *P. somniferum* var. *abnormale:* A variety not infrequent in neglected poppy fields. Flowers small, streaked with dull green and red, the petals much crumpled, and never expanding fully, capsules roundish-oblong, opening by pores under the stigma.

The above varieties, though very poor drug producers in their natural state, affording only two drug-yielding incisions, can be much improved by cultivation.

IV. Cultivated varieties of poppy

There appears to be at present no comprehensive classification of the varieties of the plant *P. somniferum*. Professor Duston sent some plants to the Royal Botanic Gardens, Kew, for their classification but attempts to divide the specimens into mutually exclusive groups were unsuccessful and it was reported that a satisfactory classification of the various forms could only be accomplished in the field by a careful observer and a judicious cultivator. Since then, so far as I know, no further attempts have been made to classify them. On the other hand, due to cross fertilization of different varieties, a number of hybrids and new races may have come into being.

Broadly speaking, the many varieties of Indian opium poppy may be separated into two well-defined races by the colour and texture of the capsules. One has capsules of an opaque green in deeper or paler shades. This comprises the subza-dheri varieties. The other has glaucous capsules, more or less densely coated with an opaque white powder. This is the sufaid-dheri group. The sufaid-dheri race may be indifferently used for late or early crop, and, with the exception perhaps of the Kaladanthi variety, the later crops may not be wanting in vegetative vigour; however they will be found to yield much less opium. Under a March sun, the latex of the subza-dheri is very rapidly exhausted and scarcely half of its normal opium content can be extracted. This species has, however, special adaptability for early sowing. The

characteristics of the two species are probably due to the difference in the texture of the capsule—that with the white powdery coating better resisting evaporation action in high temperature and a dry atmosphere than the other.

The cultivated varieties of *P. somniferum* commonly grown in Uttar Pradesh are:

1. *Teyleah variety or Telia, Haraina, Hariala, or Herera*

This is a favourite variety with many of the cultivators though far less generally grown than it deserves. For an early crop, it is certainly one of the most productive sorts. It has oblong ovate capsules with a pale, olive green colour, without powdery coating (plate I, fig. 2).

2. *Sufaid-danthi or Katha Bhabutia*

This is one of the most generally cultivated of the several varieties grown in the agency, though as a rule less productive than the teyleah variety for early crop. It is, however, far superior to it for late cropping.

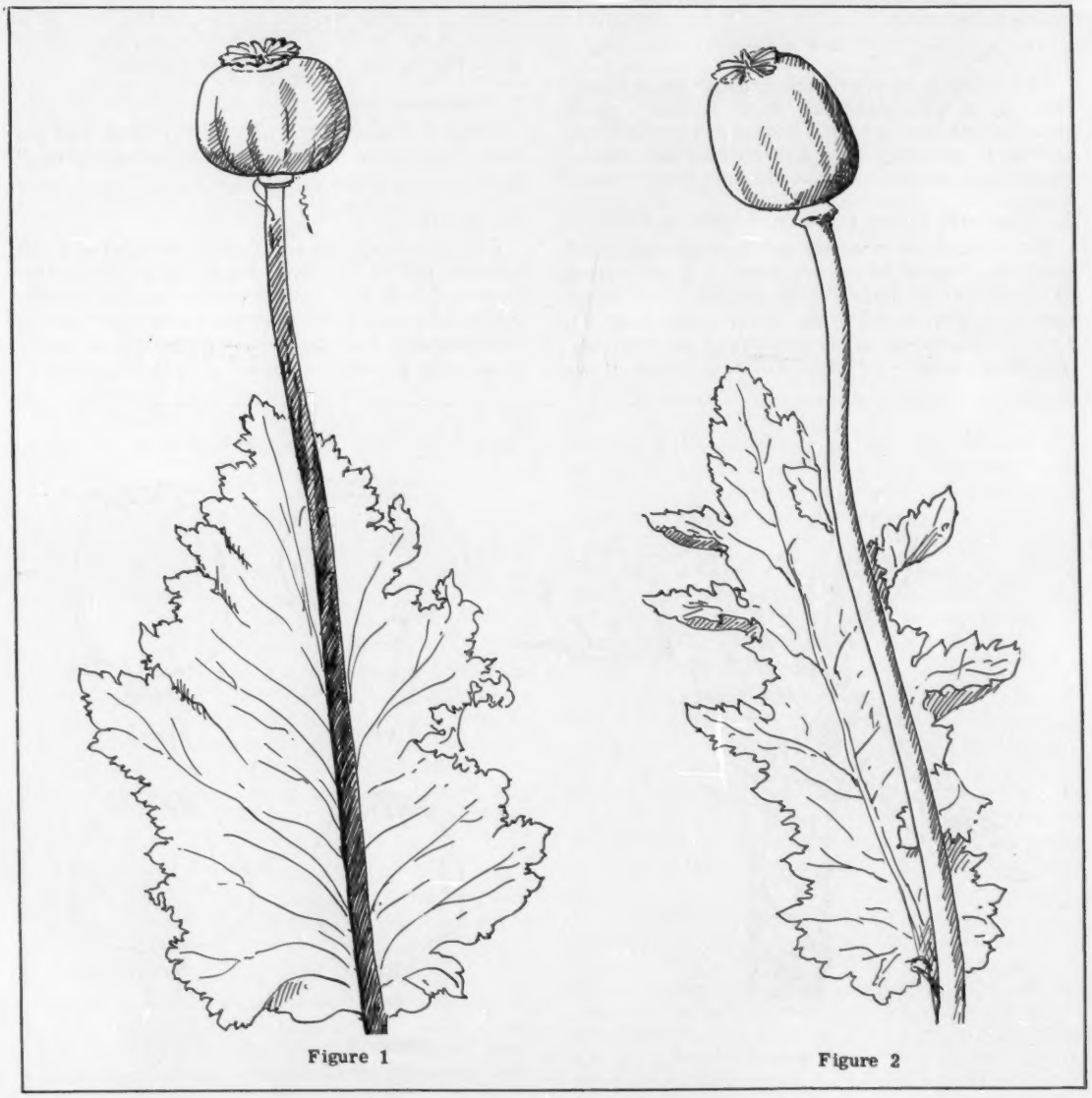

Figure 1

Figure 2

PLATE I

Figure 1. *A capsule with a leaf of variety* Kalidandi. *The stalk of the capsule has turned black.* Figure 2. *A capsule with a leaf of variety* Haraina

3. *Kutila, Katila or Kotila or Chansura, Ghanghabaha, Chirrah or Bhagbhora*

The varieties are better than any of those ordinarily cultivated for withstanding hailstorms and high winds, because of their much reduced and narrowly segmented foliage of thick and dense texture. They also, better than any of the other common cultivated varieties, resist the blights to which all are more or less subject. The varieties will do well in a sandy loam. The capsules are oblong-ovate and glaucous (plate II, fig. 4). The latex is red at the time of lancing. Sometimes there are bristles on the flower stalks.

4. *Choura Kutila*

This is also an excellent variety though less cultivated than any of those mentioned above. It differs chiefly from the last ones in having thinner and less narrowly and deeply cut foliage. It requires a strong and retentive clayey loam and more moisture than the other varieties.

5. *Kaladanthi, Karria, Damia, Kalidanthi, or Kalidandi*

This is an excellent variety and more generally cultivated than either of the two last named. It is well marked by the peculiar bluish-black colour acquired by the flower stalk soon after the fall of the flower (plate I, fig. 1). This is a less robust variety than any of the preceding. It produces, however, a great quantity of opium. It has a less protracted season than any of the other varieties and gives better returns as an early than a late crop. The capsules are oblong-ovate and glaucous (plate II, fig. 2), the latex slightly reddish at the time of lancing.

6. *Subza Kaladanthi or Haraina Kalidanthi*

This is a new race of the preceding variety. This variety cannot stand heat and excess of moisture in the atmosphere or the soil. It is good as an early crop on light well drained soil. Later in the season, the heat becomes too strong, the capsules shrivel and lose their colour, drying up prematurely and yielding little opium (plate II, fig. 3). It differs from the preceding varieties in having capsules of an olive green colour.

7. *Kalidanthi Baunia*

Same as Kalidandi but with smaller plants and produces more opium than the Kalidandi variety (plate II, fig. 5).

8. *Monoria*

Produces a large amount of opium but requires a well-manured soil of the strong clayey-loam sort. In light sandy soil it is less productive, the capsules are also smaller, of an ovate-oblong shape, and they are scarcely distinguishable from the common sufaid-dheri variety. It has large, roundish, ovate and glaucous capsules.

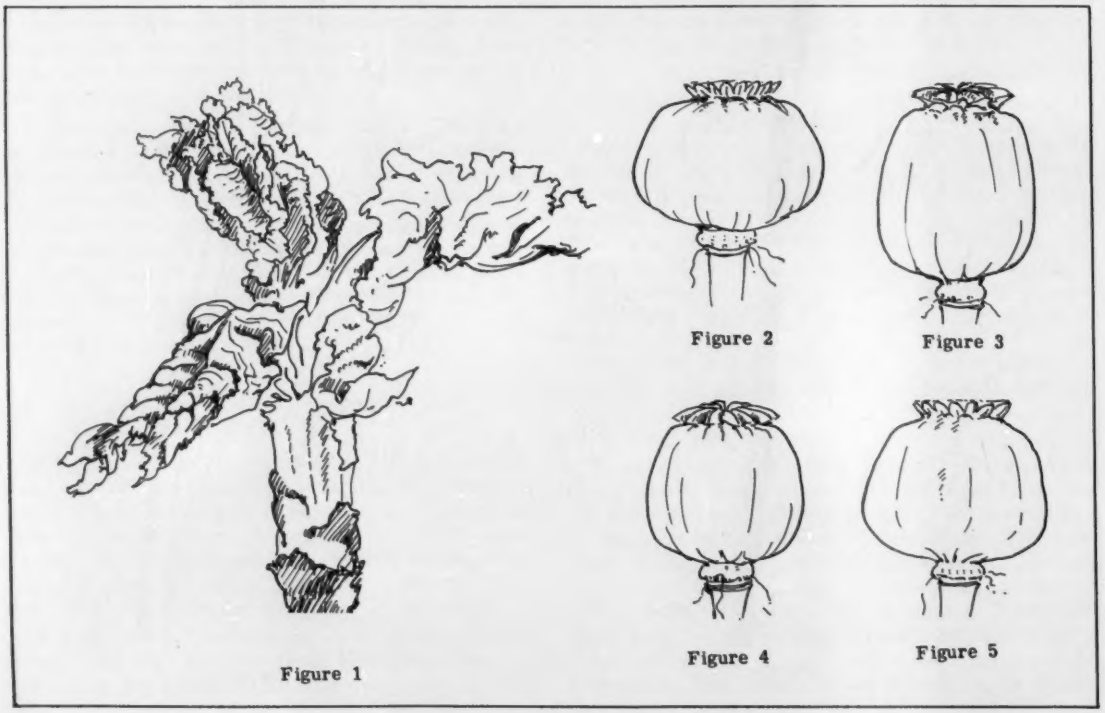

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

PLATE II

Figure 1. *A diseased plant affected by leaf curl disease. The leaf can be seen entirely twisted with the deformed condition.* Figures 2 to 5. *Different kinds of capsules from different varieties*

9. *Dheri-Danthi*

This is a new race, derived from the common sufaid-dheri. It is much less subject to the common poppy blight than any of the old varieties. However, it does not produce much opium but its opium contains a high percentage of morphine. This is an important property aside from the comparative blight immunity. Its several good qualities recommend it for experiments on a small scale with a view to its selective improvement.

10. *Variegated poppy*

This is another new race of the sufaid-dheri variety which is little affected by blights and pests. This important quality is attributable to the more highly oxygenized state of the tissues than that of the normal forms. It is quite possible that by experiment and selection it may be developed into a good opium producer.

11. *Sufaid-danthi Monoria*

This is an excellent hybrid, very robust and producing large and uniform capsules of a roundish-oblong shape.

12. *Monaria Teyleash*

This is also a hybrid which may become a good opium producer. It resembles its female parent Monoria in general appearance and form of capsule, while the texture of the capsule is quite the teyleash type, of a deep opaque green colour.

13. *Sandpha, or Dhadhua or Bhabhua*

The plants are higher than any other variety with big capsules of roundish-oblong shape. This variety yields little opium.

14. *Sahbania*

A variety grown in Eastern districts. It has long leaves with the two basal lobes falling down the leaf stalks. Capsules oblong-ovate with rough surface. Does not yield much opium.

*
* *

The Madhya Bharat and Rajasthan poppy differs considerably from the Uttar Pradesh poppy. It has a straighter stalk, simpler stem, sharply toothed leaves, of much thinner texture and the usually red or purplish coloured flowers, with fringed petals and rather large-sized oblong or ovate-oblong capsules, crowned with broad stigmatic rays. The main varieties grown in that region are:

1. *Bhatphoria or Dhaturia*

Average height of the plant 3 feet 6 inches. Capsules 3" x 2½" roundish elongated, light green. Poor opium yield.

2. *Galania*

Height 4 feet or less. Flowers white with pink or dark pink border. Size of capsule 3" x 2", round, oblong and flattened a little on top. Colour of capsule dark green. Yield more opium and less seed than the Dhaturia. Colour of opium light brown.

3. *Hybrid of the above two varieties*

Petals red and white. Often white only, but mixed also. Average height of plant about 4 feet.

4. *Ramzatak*

Flowers white and red white in colour. Capsules small and elongated, slightly flattened at the top. Size 3" x 2". Opium yield more and seed less in comparison to Dhaturia. Colour of opium dark brown turning black.

5. *Telia*

Flowers white, petals 2½" long, not furcated. Capsules elongated, light green and shining. Opium of a dark shade. Seeds white. Produces more seed than Ghotia or Chaglia.

6. *Ghotia*

Petals 2¼", white or with pink border. Capsules round, dark green. Colour of opium as in Telia. Produces less seed than Telia but more than Chaglia.

7. *Chaglia*

Petals 2½", red or pink with white dots at the bottom. Major portion of the petal is coloured. Shade of opium lighter than Nos. 1 and 2. Average yield highest of all. Seeds white.

8. *Kasturi or Tejani*

Scarlet red flowers. Very poor yield of opium. Seeds red.

V. Soil and weather

The poppy in India is grown on almost all kinds of soils, viz. clayey (Kali Matti), sandy loam (Domat I), loamysand (Domat II), sandy (Bhoor) and sandy clay but the plant prefers a soil of a sandy loam type. Such soil presents a uniform appearance and is fairly retentive and easily cultivable and productive.

The clayey type is rather hard and it is difficult to pulverize it properly for the young roots of the poppy plants to penetrate it. The sand on the other hand does not retain water which quickly percolates down and, therefore, the moisture retained is insufficient for the healthy growth of the plant.

The fertivility of the soil can be improved just by effective drainage. Insufficient tillage, root injuries of young crops, insufficient supply of sap and the surcharging of the plant with an over-diluted food due to water-logging has a most deleterious effect on the poppy. The plants become poor and stunted, the leaves are narrow of a palish green colour. The stalks are spare and simple and tend to flower prematurely giving a low amount of capsules.

To the opium poppy cultivator the weather is a very important element. A hailstorm, for example, and by no means a severe one, will ruin his crop while a heavy rainfall between the period of scarification of the capsules and the collection of the latex will leave little or none for collection. High or gusty winds are also detrimental during the opium season because they dry up the plant and thus check the exudation of latex. Whatever latex flows dries quickly so that when the capsules rub together, the opium is lost. Dull, cloudy or rainy weather tends to reduce, not only the quantity, but the quality of the drug exudations.

VI. Morphology of the poppy plant and structure of the capsule

P. somniferum

Stems from 2 to 5 feet high, simple or divided, smooth, rarely setigerous, leaves oblong or ovate, toothed and lobed, rarely pinnately lobed, from 4 to 15 inches long by 1½ to 9½ inches broad (plate V, fig. 1). Flower from 2 to 8 inches in diameter, white to various shades of purple to scarlet, sepals 2, petals 4 entire, toothed to deeply fringed (plate VI, fig. 1), capsule ovate to oblong or roundish to ovate, stigmas 3 to 16, radiating, sessile, and crowning the top of the ovary, seeds whitish to purply black.

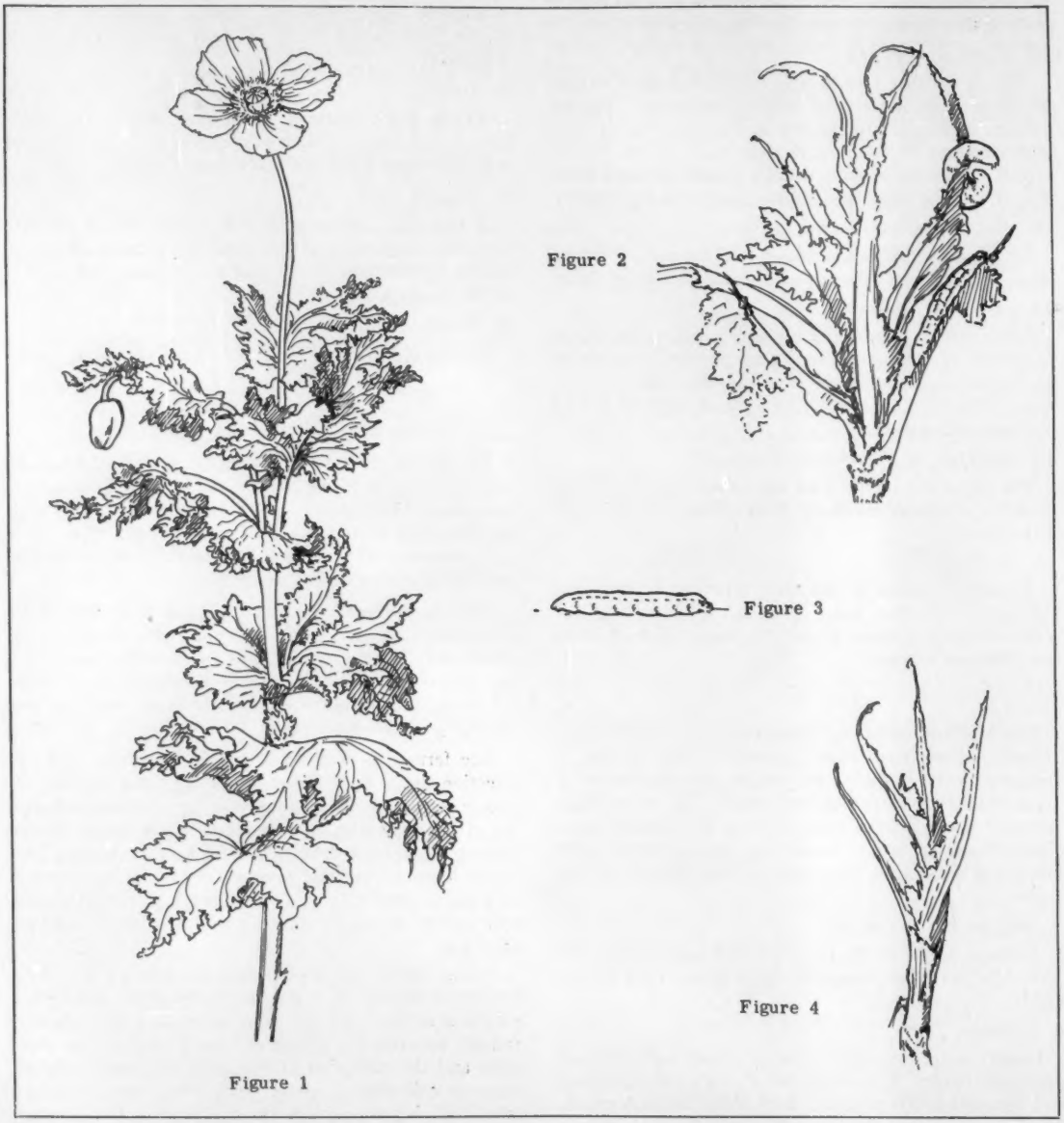

Figure 1

Figure 2

Figure 3

Figure 4

PLATE III

Figure 1. *A poppy plant of the variety* Katila. *The leaves are alternate and highly segmented with a terminal flower. A bud can also be seen coming out of the axil of the leaf.* Figure 2. *A plant being eaten by the cutworm. Two cutworms can be seen in the figure. One is actually clipping the leaf.* Figure 3. *A cutworm.* Figure 4. *A plant destroyed by cutworm. The leaf, except for the midrib, has been eaten away*

The pericarp of the capsule consists of three distinct layers (plate VI, fig. 3), the outer of epidermal tissue, forming the skin (technically called the epicarp), the middle one composed of several layers of hexagonal cellular tissue (technically forming the mesocarp), and lastly the inner, and, from our point of view, most important layer (technically called the endocarp), composed of loose cellular tissue permeated by a fine network of reticulated and dotted vessels, forming probably organs of absorption. The stigmatic ray is composed of four distinct layers, first a deep layer of loose cellular tissue, invaded by a network of spiral and reticulated vessels from the midrib. The epicarp is formed of a single layer of colourless thick walled vessels, ultimately forming an almost horny membrane with numerous stomata. The middle or mesocarpa zone, consists of a loose network of hexagonal cells, the intercellular spaces of which are everywhere invaded by the latex and absorbent vessels —first by the latex or drug secreting vessels. A longitudinal section of the pericarp will show an irregular but compact network of vessels of which the majority are from 500th to 800th inch in diameter and thus afford a considerable drug secreting capacity. This system is much less developed in the capsules of the plants with low opium yield. The latex is generally present throughout the plant in articulated, laticiferous tubes, frequently having sieve plates on the transverse or lateral walls.

VII. Area under poppy cultivation and its yield

The poppy in India is grown in Uttar Pradesh, Madhya Bharat, Rajasthan and in Himachal Pradesh. The total area under poppy cultivation in the opium seasons 1951-52 and 1952-53 with the total produce and its average yield is given below:

	Total area in acres		*Total produce kgm.*		*Average yield per acre*	
	1951-52	*1952-53*	*1951-52*	*1952-53*	*1951-52*	*1952-53*
Uttar Pradesh	33,776	30,759	206,481	201,703	6.11	6.55
Madhya Bharat	10,152	30,717	65,259	249,643	6.43	8.31
Rajasthan	10,089	20,804	75,171	172,289	6.60	8.28
Himachal Pradesh	2,197	2,046	3,546	3,173	1.62	1.55
Total	56,214	83,626	350,457	626,808	6.23	7.50

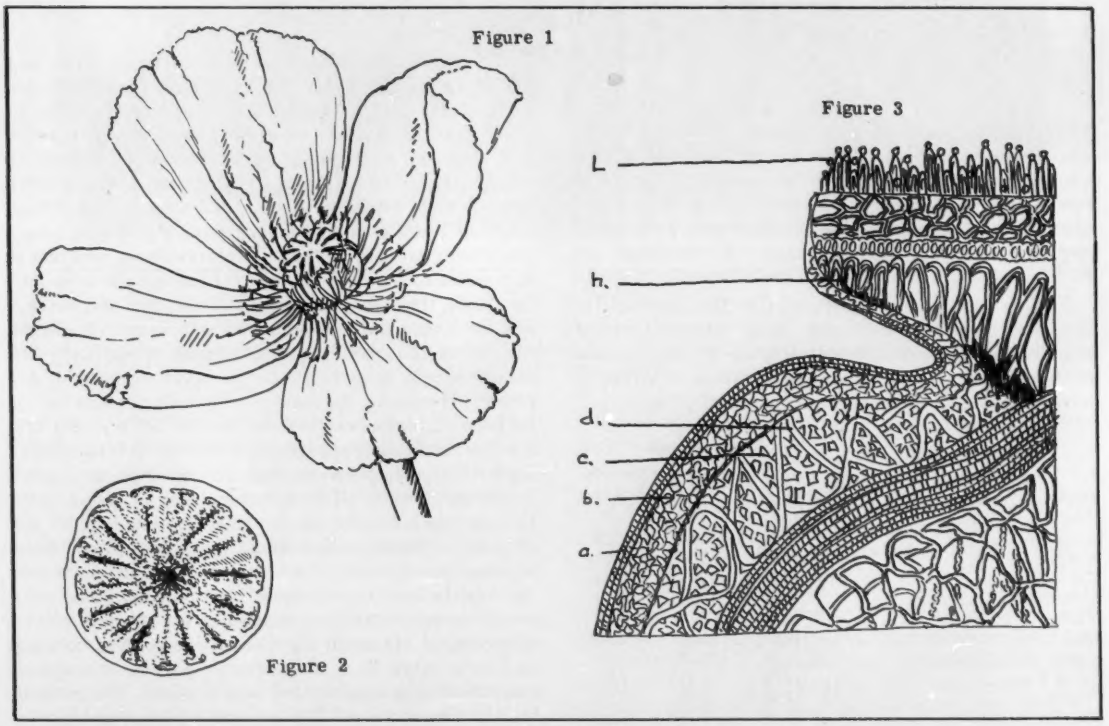

Plate IV

Figure 1. *A poppy flower with four petals. The sepals have dropped off. The young capsule can be seen surrounded by a number of antheridia.* Figure 2. *Transverse section of a capsule showing the position of seed.* Figure 3. *A diagrammatic section of a portion of the capsule (after Scott).* a. *Epidermis.* b. *Middle zone of pericarp.* c. *Endocarp.* d. *Milk system of endocarp.* h. *Lower stigmatic layer.* l. *Pollen grains*

The total area under cultivation in the year 1953-54 is as follows:

Acres	*1953-54*
Uttar Pradesh	19,098
Madhya Bharat	19,846
Rajasthan	12,775
Himachal Pradesh	1,211
TOTAL	52,930

VIII. Alkaloid contents of Indian opium and its chief characteristics in comparison with opium of other countries

As early as 1907 the attention of the Government of India was directed to the possibility of increasing the demand for Indian opium for medicinal purposes. The greater part of this trade was at that time in the hands of Turkey where the opium produced was much richer in morphine content than the Indian product; nevertheless, the Government of India thought it possible that this difficulty might be surmounted. One of the reasons why Indian opium was so much inferior in this respect to the Turkish product appeared to be that the opium, from which Indian medicinal supplies were made, was selected in the most haphazard way. Nothing was then really known regarding the locality from which it came, from what seed or in what manner it was grown, or for what reasons the plants had been considered suitable for selection.

A large number of samples of opium collected in 1909 from the various opium growing districts of India were sent to the Imperial Institute in London. The systematic investigation of Indian opium by the Institute conclusively showed that much of the opium produced in India contained sufficiently high percentage of morphine to render the drug suitable for medicinal use in Europe or for the manufacture of opium alkaloids.

Further samples were dispatched to the Imperial Institute in 1915. Some of the results obtained in the examination of these selected samples are summarized in the following table in which the opium is arranged according to the percentage of morphine present:

	In dry opium		
Variety of poppy	*Morphine*	*Codeine*	*Narcotine*
Posti	14.25	2.91	7.61
Katila	13.62	1.86	5.74
Baunia	13.44	3.93	5.27
Karria	13.27	3.35	7.01
Katila	12.65	2.91	7.54
Bharbharwa	12.54	3.24	6.19
Katila	12.34	3.24	7.12
Desi	12.07	3.72	4.86
Katila and Telia	11.91	3.57	6.40
Safed Posta	11.83	2.81	5.96
Maghaiya	11.80	3.46	4.90
Hariala	11.48	3.13	5.34
Safeda	11.45	3.67	6.64
Safed danthi	11.16	3.54	5.78
Kotila	10.98	2.81	7.13
Baunia	9.57	3.98	4.52
AVERAGE	11.37	3.26	6.06

From the above results it will be seen that the percentage of morphine varied from 9.57 to 14.25, the average being 11.37. The average amount of codeine present in these samples comes to 3.26 and that of narcotine 6.06. Taken as a whole, therefore, the composition of Indian opium is very satisfactory. Out of the samples examined, opium from the Katila poppy was found to be of very good quality, the percentage of morphine ranging from 11.59 to 13.62. Opium from the "Baunia" poppy gave from 9.57 to 13.44 per cent of morphine with an average of 11.13 per cent, and that from "Posti" poppy gave from 9.34 to 14.25 per cent.

The comparison of the samples of opium from the same variety of poppy does not permit any satisfactory conclusion to be drawn as to the cause of the variation in the amount of morphine present, and it can only be concluded that apart from variety there are other conditions which have an important influence on the quality.

The results, however, clearly and conclusively indicate that opium of exceptionally good quality can be obtained in India.

Indian opium has a great advantage over Turkish and Iranian opium, in so far as Turkish opium contains less than 1 per cent of codeine on the average, and Iranian opium about 2.5 per cent, whereas Indian opium, apart from its high morphine content, gives an average of 3.5 per cent of codeine.

The results encouraged the Government of India and the Opium Department and, therefore, from 1916 onwards further experiments were conducted in order to determine the varieties of poppy, the kinds of manure and soils, and the methods of cultivation best suited for the production of opium of good quality. Useful results have been obtained. It is now definitively proved that the first and second exudations from the lanced poppy head bring with them the bulk of morphine, and that it is possible to divide the whole produce of the crop into two parts, the first half for medical purposes and the second for Excise purposes. The first scarification is always the richest, the second is distinctly poor in morphine and in subsequent scratchings the morphine gradually decreases. Herein lay the reasons why Indian opium had so far been said to be poor in morphine. In Turkey, only one scarification is made apparently, when the cultivator catering for the medical market obtains by his single serpentine scarification nearly all the opium suitable for his purpose. In India, the cultivator rarely makes less than four. When all these scratchings including the first one, are mixed together, even though these may be rich in morphine, the total bulk of opium becomes low in morphine content. It is now established that India can produce plenty of medicinal opium of high morphine content so long as care is taken that cultivators do not mix the opium from the first and subsequent scarifications. The method of collecting opium of first and subsequent lancings has been practised by the cultivators in India for the last two years with good results. We can supply opium to all the countries in the world who want it from India with any morphine percentage ranging from 9 to over 12 per cent. Last year medicinal opium was supplied by

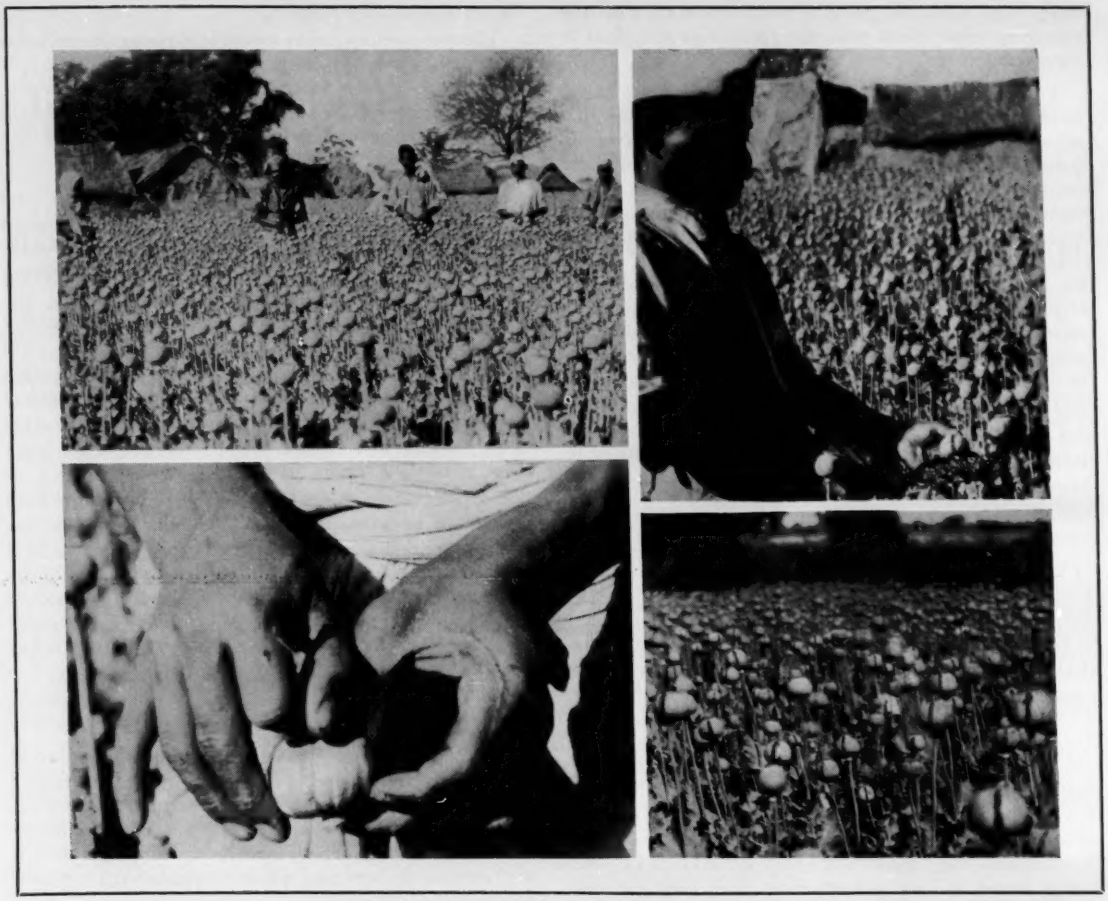

PLATE V

(Top left) *Ripe field ready for lancing. Five persons are going in a line lancing the capsule.* (Lower left) *A close-up view of the method of holding the capsule and lancing it.* (Top right) *Latex being collected in a shovel.* (Lower right) *The field after the capsules have been lanced*

us to the United States, the United Kingdom and France. These countries had nothing but good words to say both for the quality of the drug supplied, the method of packing and dispatching and the promptness in executing all the orders.

Work has also been carried out to determine whether the amount of codeine and narcotine also varies in the opium of successive lancings and increases in proportion with the falling off in morphine content in the successive lancings, since codeine and morphine are very similar in chemical constitution. In general, however, it is seen that the percentage of codeine does not vary very much in the opium of successive lancings. It shows a slight increase in the later lancings but the increase is not sufficient to account for the falling off in the morphine content. Narcotine, however, falls off in a manner very similar to what we have observed in the case of morphine but the falling off is not so marked.

It follows that the opium of the first and second lancings will still contain practically as much codeine as ordinary Indian opium and thereby will keep up the reputation of Indian opium for high codeine content.

IX. Enemies of the poppy plant

The poppy is a delicate plant and needs utmost care and attention during the entire period of its growth from the seedling stage until the capsules ripen. Unfortunately, the poppy plant has many enemies against which it has to fight during its life period. Apart from natural calamities like sunburning, hail and frost, it has also to suffer from many insects, birds and other animals. Fungus and virus diseases also take their toll.

No sooner do the seeds germinate and the seedlings sprout two to four leaves, than a small insect locally known as *Dhirku* or *Gadhiya* starts the trouble. This

insect hops from one plant to another and clips off the young terminal shoot with the result that the plant is incapacitated for normal growth.

The cutworm (plate V, fig. 3) often commits havoc on the growing crop. Its ravages extend in the dry season from November to January. These cutworms remain burrowed in the soil during the day and come out only at night to carry on their depredations. In the night I have seen hundreds of these worms on the leaves of the plants which they cut (plate V, fig. 2). The entire leaf is eaten away by these cutworms except the midrib (plate V, fig. 4) and the affected plants die after a few days. The loss from this worm is sometimes enormous. The only remedy is to flood the fields with water. By doing so these cutworms float on the surface and are picked by their enemies—the birds.

The cricket, *Gryllotalpa vulgaris* is often a very serious pest, cutting over with its mandibles plants almost fully grown.

The caterpillars of a moth also prove very serious enemies to the growing crops, their ravages extending from December to February. In this case also irrigation dislodges them from their soil haunts and they are eaten away by their natural enemies: the Indian crow and *myna.*

Rats, rabbits, monkeys, blue bulls and parrots also destroy the crop considerably. The poor cultivator has to save his crop during the day from monkeys and parrots and during the night from rabbits and blue bulls. In good irrigated fields, rats are not a great menace because they are easily dislodged from poppy fields. They run to make their homes in an adjoining field where they find less danger from water and better food like wheat or gram. The damage from blue bulls is sometimes very great. Once they get addicted to the poppy leaves and stems containing latex they will not eat anything else. Apart from eating them, they also destroy the plants by breaking them with their strong hoofs while running through fields. Hindus consider it irreligious to kill them. They consider killing it as bad as killing a cow.

In sunburning (*Moorka* or *Joorka*), the leaves get dried and wither, with more or less discoloured purply-black or brownish veins, the pith decaying from above downward. Plants exhibit these symptoms, both in poor and rich soils, when the weather is hot and there is a deficiency of moisture in the soil. Under these conditions the roots fail to keep pace with the leaf transpiration.

Frost is also sometimes very destructive. During heavy frost the thermal balance of the protoplasm of the cells is lost. The protoplasm, in such cases, shrinks and the cells die. The only remedy for this appears to be to water the fields profusely the morning after the frost when the plants will again try to regain their proper balance and the crop may be saved. There is hardly any remedy against hail except the prayers of the cultivators.

Injuries caused by fungi

The most serious poppy mould is *Peronospora arborescens.* It is, however, not so destructive as its other species *Peronospora infestens* to the potato. The less succulent structure of the poppy is evidently unfavourable to any rapid or general extension of the mycelium. The disease is commonly known as *Chirrah* or *Agiya.*

Dactylium roseum

The pale rose coloured patches of this thread mould are very common on the poppy during moist, warm weather. In the opium godowns and, in fact, on opium everywhere, it finds a favourite media covering the surface with its rosy web of mycelia when left for any time undisturbed (plate IV, fig. 2).

Other species of fungi reported on the poppy plants are *Trichoderma viride, Sporotrichum Sp., Cladosporium herbarium, Rhizomorpha Sp., Mucor mucedo, Aregma moniliforme* and *Phelipea indica.* None of these, however, cause any serious damage to the crop.

Poppy plants suffering from leaf curl disease are very frequently found in the fields. Sometimes it is devastating. The symptoms are identical to the potato and tobacco mosaic and it is surmised that this may also be a virus disease (plate II, fig. 1). The only method of eradication is to pluck the diseased plants as they appear and burn them. Plants with gangrene and root canker are also occasionally met with.

X. Technical work in progress

The poppy crop, as grown by cultivators, consists of a wonderful assemblage of types intermingled with each other and intercrossed and the work of sorting these out and testing the relative value of each appears to be necessary. The cultivator's field involves too large a scope for the personal element and is not a suitable basis for comparative experiments.

It is already possible to say that there is a very wide divergence between different races with regard to the morphine content of their opium. The highest figure of morphine obtained from a pure race is over 14 per cent. With diminishing consumption of opium every year by 10 per cent with a view to completely prohibit its use for quasi-medical purposes by the year 1959, the excise opium in India will go out of market. Our main effort at the present moment is, therefore, to find out those varieties which will give opium of high morphine percentage for medicinal purposes. At the same time we are not to lose sight of the cultivator and his profit. It is, therefore, equally essential to isolate a race which, with a high morphine content, will also give a high average yield. This will not only be beneficial to the cultivator but also to the Government because the land thus saved will be utilized for growing other crops like wheat, gram, etc. Experiments on large scale are, therefore, being conducted to achieve this object. Attempts will also be made to discover a variety which, with all the above advantages, may also be disease resistant.

Opium in Pakistan

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When the Indian sub-continent was divided in 1947 into the two Dominions of India and Pakistan, Pakistan had many problems of administration to face which were at that time more pressing than the setting up of a machinery to control the opium traffic. But this traffic is of such importance both in the life of the country and in its international relations that it was not long before the outlines of a system of control began to be formed.

In India the Centre had the constitutional duty of controlling the growing of the poppy and of making and distributing the opium to the provincial authorities, who in their turn controlled the retail sale to consumers through licensed shops and dealt with the preventive work which was necessary to check illicit distribution and addiction. The new State of Pakistan accepted this organization of functions.

But there was at that time no opium department under the Central Government of Pakistan, and the main growing areas were in India. Under an agreement made with India, opium was to be supplied to Pakistan from the factory at Ghazipur, in India, until March 1948. This supply was intended to maintain the existing trade, through the Central Government, which would purchase the opium, to the Provincial and State Governments, which would see to retail distribution through their licensed shops and would deal with smuggling.

A spur was applied to the organization of an opium department in Pakistan and to the desire which was already present to attain self-sufficiency in respect of this commodity by the virtual failure of the supply from India for a time. Pakistan had to take rapid steps to explore the possibilities of growing the poppy and of making her own opium: meanwhile other sources of temporary supply outside the country were also sought. In addition, the obligations of the new State to the United Nations were reviewed in order to ensure that the opium administration which was to be set up finally should be able to carry out those obligations fully.

The use of opium on the Indian sub-continent had been an ancient tradition, and there had been relatively little addiction as addiction is understood in the West. Indeed most of the use had been rather in the line of what is now called "quasi-medical use" than in that of true addiction. Medical facilities and medical education among the people were not as developed as they are in the West even in 1947, and the use of opium as a specific against abdominal illnesses, pain, and some fevers was general, especially in rural areas, and above all in those areas where excessive rainfall and flooding had rendered dysentery, malaria and kala-azar endemic.

Nevertheless Pakistan, as successor to the Government of India, determined to follow the policy of gradually reducing the use of opium and of trying to exterminate addiction properly so-called. But it was recognized that this process must be gradual; that as the executive power rested constitutionally with the Provinces and States, a policy would have to be worked out in consultation with them and after due consideration of their views; and that that policy must always regard the obligations of the country to the United Nations.

The problem therefore had a number of aspects, all of which had to be taken into account. There had to be an adequate supply—about 500 maunds a year—which had to be ensured from abroad till production could be organized in the country: eventually the supply from India was restored on a basis which recognized that the demand would be reduced progressively: experiments in cultivation were begun, while the Central Government took over the control of policy in general in the Revenue Division of the Finance Ministry. The question of forming a Narcotics Board, as had been suggested by the League of Nations, as a central authority for the control of the opium traffic was considered, and a decision was postponed till the major administrative difficulties of setting up an opium department were settled.

The control which the Government exercises is by licensing the growing of the poppy over an area which is calculated as adequate to ensure a supply sufficient for the needs of the country. The cultivators who grow under licence also come under the supervision of field staff maintained by the Government, and when the opium is ready the lancing is supervised and the product is bought for cash on weighment by Government field staff. From then, the opium is in the hands of Government until it is sold to the consumer from the Government excise shop. The field officer, who is an employee of the Central Government sends the crude opium to the central factory where it is brought to the strength and consistency required by the local Governments who buy it for their

shops. Indents are dealt with by the factory, which comprises a manufacturing section, a store and a laboratory.

Manufacture is simple. The crude opium is kneaded and exposed to the sun in large flat pans. The process continues until the opium is a dark brown colour and until the consistency has been raised to 90 per cent. The opium then has a wax-like appearance. It is moulded into square cakes, stamped and wrapped in oil paper ready for supply. A certain portion of the product is also put on one side for manufacture into medical opium powder.

The Government of Pakistan had to find areas where soil and climatic conditions were suitable for the growing of opium. They had to find a staff who had the necessary knowledge and experience for the field work, and they had to persuade cultivators to take up the licensed cultivation of opium as a cash crop—in substitution for other crops or as an alternative to them where this was possible.

A nucleus of staff was found from the Muslim officers of the old Opium Department who had opted to serve Pakistan. But the first experiment in production took place in the West Punjab, at the suggestion of the Government of that Province, under the aegis of the Co-operative Farming staff of the provincial Government. It was thought that conditions for the cultivation of the poppy appeared to be favourable in the West Punjab and the Central Government agreed to the experiment. It should be noticed that the cultivation of the poppy in what is now East Pakistan had been prohibited by law since 1839, and it was not felt that experiments in that area had any reasonable prospect of success.

In 1948, therefore, 491 acres were planted with poppy seed in the West Punjab; but the experiment was a failure. The crop failed entirely in 231 acres and the yield in the remainder was only 31.313 seers (a seer is a little over 2 lbs.) of raw opium at 70 per cent consistency. It would not have been over-optimistic to have expected a yield of 3,000 seers from the acreage planted. Early in 1949, the Central Government was able to send experienced staff to give instructions in the best method of lancing; by that time it was too late for their directions to make a material difference in the yield.

The experiment was analysed, and the conclusion was reached that the failure was due to a number of causes. Inexperienced supervising staff, late sowing, poor seed, and lack both of knowledge and of real enthusiasm among the cultivators were the main reasons.

The first experiment took place in the Montgomery District (see map) and not deterred by the failure the Central Government now decided to take up the battle themselves, still in the Punjab. In the second experiment 824 acres were eventually sown, although the original intention had been to place as much as 4,600 acres under cultivation; an area which it was thought would meet the whole need of the country. If it be thought that this was over-ambitious as an experiment in a rather difficult form of agriculture which had been hitherto virtually unknown in Pakistan, it must be remembered that necessity was driving the Government. It was thought at this time that there might be no supply from India at all, and the prospects of obtaining a supply from other overseas sources were not good.

Pakistan. Raw opium from field being received by officer

The second experiment also failed. Cultivators were not enthusiastic; sowing was again late; only a poor quality of seed was available, since standard seed could not be procured from India, while the water supply in the main canals was disrupted at the time at which it was most needed. Abnormal weather conditions were encountered in the winter, with rain and hail which did much damage to growth and to standing crops. About 300 acres failed altogether, while the rest of the land gave a yield of only 254.555 seers of raw opium.

Nevertheless, the conclusion was reached from the two failures that it was practicable to grow opium in West Pakistan, granted certain conditions. Soil and climatic conditions were normally favourable; better supervision could be provided and if cultivators could be supplied with first quality seed and would themselves take a live interest in the crop, it was felt that a successful result could be obtained. A third experiment was therefore sanctioned for the year 1950/51; again the West Punjab was to be the scene.

For a number of reasons, there was yet another partial failure, the product being 784.68 seers of opium at 70 per cent consistency from 982 acres of cultivation. The seed was again not satisfactory, and cultivators who lacked the skill and knowledge to make a success of the growing and of the delicate operation of lancing did not show the interest that was needed for satisfac-

tory results. But the necessity to produce opium still existed: a supply from India had been restored, but both on grounds of conservation of exchange, and of the need for self-sufficiency it was decided that the effort could not be given up. But the Government of Pakistan decided also to shift its ground to two new areas—the North West Frontier Province and the State of Bahawalpur.

The new experiment was limited in extent: an area of 59 acres in the Mardan district of the N.W.F.P. and of 50 acres in Rahimyarkhan in Bahawalpur State were sown. 19 acres and 21 acres in Mardan yielded 154.312 seers of raw opium at 70 per cent consistency, while at Rahimyarkhan the yield was negligible. An analysis of the Mardan experiment showed that the yield per acre of productive land was 4.7 seers, while some fields gave 8 seers, and two gave as high a figure as 16 seers, an acre. It was therefore decided that in 1952/53 cultivation would be carried on again in the N.W.F.P., on an extended scale, and that the experiment in Bahawalpur State would not be repeated.

In 1952/53, therefore, 756 acres were cultivated successfully in the N.W.F.P. and certain adjoining areas in the north of the Punjab, producing about 128 maunds of raw opium at 70 per cent consistency. This represents between 25 per cent and 30 per cent of the total demand of the country, and the result may be treated as a considerable success when it is remembered that the demand is to be reduced year by year under the policy of steady diminution of supply which has already been accepted by Pakistan. The average yield was 6.75 seers an acre, which is satisfactory. During the current season, again, which began in October 1953, cultivation was started in the N.W.F.P. and the adjoining areas of the Punjab. 2,000 acres have been sown. Results will be known by the end of June 1954. At the time at which this paper is being written it is anticipated that the cultivation will be successful, and it is already hoped that all the demand in Pakistan will be supplied by local cultivation by 1956/57. Meanwhile the supply from India for the balance of the demand is assured.

As an essential part of the plan for the production of opium in the country, a factory was set up in the suburbs of Lahore in 1950. The factory manufactures excise opium and opium powder for medical use by the process which has already been described. The laboratory has been equipped to carry out qualitative and quantitive analyses of all types of opium and opium products and it can also manufacture crude morphine. This factory was equipped locally by local manufacturers of machinery and equipment, and is able to prepare all the opium which Pakistan requires.

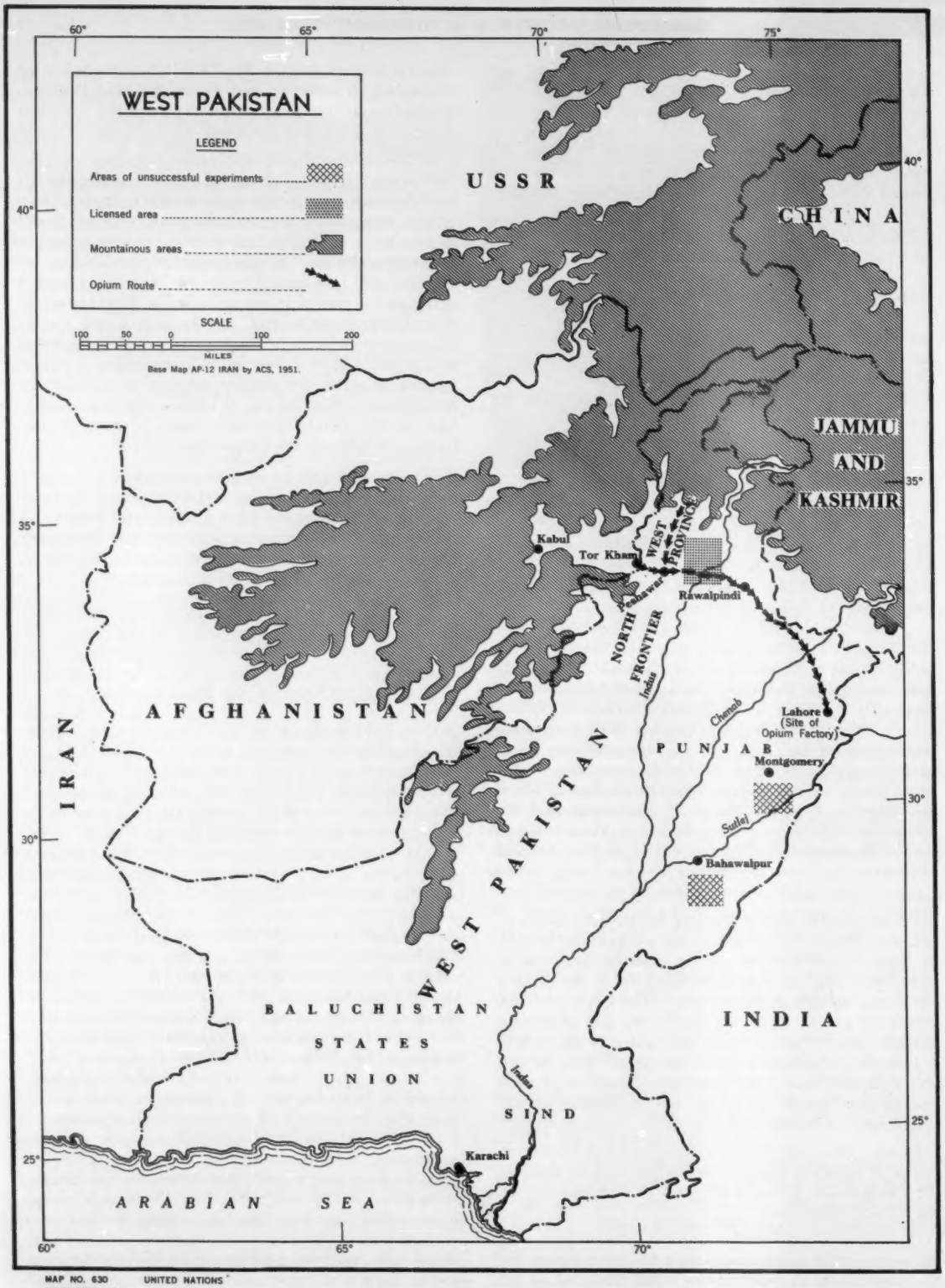
In addition, experimental cultivation of different varieties of opium is being carried on on a small scale by the Government Forest College at Abbottabad and at the Punjab University.

It may be asked whether this persistent effort, and the setting up of regular cultivation and manufacture by the Government of Pakistan are worth while, when the country is committed to the United Nations policy of eradication of addiction and, under the 1953 Protocol, elimination of quasi-medical use in a limited time. But there is no doubt that the effort was both desirable and necessary.

There is a large legitimate demand in the country—it has been estimated in this paper at 500 maunds a year. If this demand is not met under proper control, it will be met by smuggling opium over the mountain border in the North West. The elimination of the social use of the drug will take time. During that time it is essential that growing, transport and manufacture should be under strict Government control. On the supposition that in 15 years the drug can be eliminated from all but medical use, it will still be necessary to manufacture a certain amount of opium for medical use, and to manufacture derivatives for medical use. What has been done, therefore, is not merely necessary under present circumstances: it looks to the future also.

Side by side with its efforts to introduce a properly regulated system of growing and distribution, the Government of Pakistan and the Provincial and State Governments have held their legal system under review since 1947, by correspondence, by meetings and in early April, by a full scale conference held at Lahore.

At the time at which Pakistan came into being, opium smoking was not legally prohibited in any unit of the country. There were only restrictive enactments in the Provinces and States. On the advice of the Government of Pakistan, the units of the Federation have passed legislation to prohibit the smoking of opium in 8 out of 9 units. Legislation in the remaining unit will be placed before its Legislature in the autumn of this year. In respect of opium eating, it has already been indicated that there is not a great deal of addiction, as the term is understood in the West, but that the drug is taken by the mouth by ancient tradition in many parts of the country as a medicine. There is not much evidence as to the extent to which this practice is deleterious. It is hoped to have an inquiry made into this aspect of the problem in the near future. Meanwhile, efforts are also being pursued to improve the standards of medical services throughout the country, as a *sine qua non* for the removal of the old traditional medical use of opium. This will take time: but there is a measure of agreement among the Provincial and State Governments, and with the Central Government, that legislative steps must also be initiated for stricter control of the opium eating habit, in whatever form it manifests itself, and that the control should be under medical supervision, so organized as to stop the spread of the habit and gradually to eliminate it. The drafting of a set of Rules under existing legislation is being dealt with by the Central Government, in consultation with the Provinces and States. These Rules will be designed to limit the issue of excise opium—other than that which is used for medical purposes properly understood—to consumers who are registered with and have a ration card issued by the local medical authority. After a fixed date no further con-



MAP NO. 630 UNITED NATIONS
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sumers may be registered: automatically, in time, the registered consumer will disappear.

The provision of statistics of the traffic in opium to the United Nations is the responsibility of the Central Government of Pakistan. But it will have been seen that while the provision of material in respect of the cultivation and distribution of opium so far as those functions are exercised by the Central Government is simple, material in respect of distribution in detail and of consumption must derive from the Provinces and States. These units also provide information on the illicit traffic, which falls within their jurisdiction, as does the revenue derived from the sale of excise opium. The question of organizing a fully fledged central authority which would have the sole function of dealing with international and internal relations on opium has engaged the attention of Governments in this country for some time. It is now held strongly and definitely that there should be such an authority, although its functions could not be allowed to impinge upon any functions which the Constitution lays upon Provincial or State Governments. The plan for the formation of a Central Narcotics Board is therefore being pursued, with the intention that such a Board, one of the main duties of which would be to watch the implementing of United Nations engagements and the provision of statistics should come into being as soon as possible.

Finally, a word should be said on the illicit traffic as it affects Pakistan. In 1947, apart from uncontrolled growing in Pakistan itself, which was not of great importance, there were areas outside the administrative control of Pakistan where a good deal of opium was produced. In India there is a system of regulation on which the Pakistan system which has been described in this paper is largely based. In the tribal areas adjoining the North West Frontier Province of Pakistan, the ordinary law of the country did not apply, and there was no restriction on the cultivation of the poppy, for consumption or export. Beyond the borders of tribal territory, again, there were countries where the poppy was extensively cultivated. Opium came into Pakistan by devious routes over a frontier which was largely mountain and desert, and found a lucrative market both in the country and beyond it. There has been, in fact, from very early ages an opium road which leads into Pakistan from the North West, and through it into India and beyond.

It is hoped that the introduction of cultivation sufficient to meet all the legitimate needs of the country will help to check the illicit traffic by supplying the market: in addition, the main producing area in tribal territory has now come within the scope of the central scheme of licensed growing, which represents a signal advance in control. Active preventive operations on their borders and in their territory are also being carried on by the Governments which are mainly concerned, those of the N.W.F.P. and the Punjab. It is hoped, further, that the application of the policy of restriction leading to elimination gradually will not create an increased demand on the illicit market. *Festina lente* is in this respect a prudent and a necessary policy; the people of the North West are well aware of the economic advantages of sale to the Central Government at a fixed price; and of the profits of smuggling—at a risk—if the policy of the Government is not a wise one.

Poppy crop under cultivation

Out of the confusion of 1947 has emerged, therefore, in this sphere as elsewhere in Pakistan, a coherent policy: a plan which takes account both of obligations in the international sphere and of the internal constitution of Pakistan; and a determination to carry out this plan. There have been many obstacles and many setbacks; but the indications for the future are that Pakistan is in a fair way to attain a type and degree of regulation which will be in the fullest accord with accepted international practice.

Adulteration of Mexican Opium

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Introduction

Although the dried latex from the unripe capsules of *Papaver somniferum L.* contains neither starch nor strontium sulphate, these two substances are very often found in opium seized by the Office of Attorney General of the Republic of Mexico, and more particularly in opium originating in the State of Hidalgo.

This paper is concerned with the quantitative determination of the starch and celestite contained in these specific Hidalgo opiums.

Methods

1. Determination of moisture content

One gramme of opium is spread out in a previously-weighed dish, and placed in a vacuum desiccator with phosphorus pentoxide until the weight remains constant. This operation should be performed with ten samples in order to obtain figures from which an average may be derived. The mean result yields a water content of 11.64 per cent in this adulterated opium.

2. Microscopic evaluation of starch content

One gramme of dry opium powder is triturated in a mortar containing two cubic centimetres of 96 degrees ethyl alcohol made up to ten cubic centimetres with simple syrup (850 grammes of sucrose made up with water to 1,000 cc), thoroughly mixed, and examined under the microscope on a Spencer slide.

The operation is repeated two or three times with other specimens and the average figure obtained. The number of starch grain multiplied by 10,000 yields the grain count per cubic centimetre, and the result, multiplied by ten, is the number of grains of starch per gramme of dry opium.

The average number of grains counted on the Spencer slide was 1.5 so that one gramme of dry opium contains 150,000 grains of starch.

Note. The starch is rendered distinguishable by an iodine reagent.

3. Chemical evaluation of starch content

Ten grammes of dry opium powder are exhausted with cold water, the residue is placed in a flask and 200 cc of 80 degrees ethyl alcohol containing 5 per cent of potassium hydroxide are added. It is then heated and refluxed in a water bath for twenty minutes. It is filtered hot and the residue is washed in 90 degrees ethyl alcohol, at heat, until the liquid becomes almost colourless. The alcohol fractions are jointly evaporated to dryness *in vacuo*. 200 cc of water and 16 cc of hydrochloric acid of specific gravity 1.16 are added to the residue and the whole is refluxed for three hours. It is then cooled, and neutralized to pH 7 with sodium carbonate. After filtering, it is diluted with water to 300 cc. The liquid is divided into three 100-cc portions and the reducing sugar content of each is determined by means of Fehling's solution. By this process the pentosans, such as starch and other carbohydrates which undergo hydrolysis when boiled in a hydrochloric medium, are counted so that the method is not very accurate.

The percentage of starch found was 37.4.

Calcining loss and ash analysis

100 grammes of impure opium yield 12.5 per cent of ash by calcination.

The composition of the ash is as follows:

	Per cent
K_2O	1.01
Na_2O	2.17
CaO	6.72
SrO	40.21
Mg	0.74
Fe_2O_3	1.21
Al_2O_3	1.14
SiO_2	16.11

Discussion

It is very important from the legal viewpoint to determine the substances used to adulterate opium in Mexico, because their identification makes it possible to ascertain geographic regions in which illicit traffic in the drug is carried on. In the present instance strontium sulphate was found in the ash of the poppy juice.

In Mexico, strontium sulphate is usually found in limestones and sandstones and mainly in the localities of Amajac, Jaso and El Salto, all of which are in the state of Hidalgo.

Celestite, or orthorhombic celestine, also occurs in fibrous, radiate and globular form. Its lustre may be glassy or pearly. Colour white, often bluish. Scrapings

white, hardness from 3 to 3.5 and specific weight from 3.95 to 3.97; fusibility 3; it imparts a crimson colour to the flame. (The fusibility of 3 is determined by that of the edges, as in actinolite.)

Opium adulterated with earth from the state of Hidalgo (celestite) contains this latter substance and wheat starch (fecula extracted from the caryopsides of the *Triticum vulgare Villars*).

The microscope reveals this powder to be composed of disc-shaped, lenticular grains of widely varied size. The smallest are irregular; the largest appear circular when viewed from the front and as greatly elongated ellipses from the side. Their greatest diameter is five one-hundredths of a millimetre. The hilum is scarcely visible; it is usually situated in the middle of the grain and surrounded by very thin, concentric layers.

Summary

1. A case of adulteration of Mexican opium is described.

2. An account is given of the methods employed to analyse the impurities.

3. On the evidence of the analytical results the geographic location of the illicit traffic in opium can be identified.

Part IIIA. The Ultraviolet Spectrophotometric Method

By Charles G. Farmilo

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1. Introduction, statement of objective

Absorption spectrophotometry offers a means of analysis which supplements the information obtainable by colour and crystal tests and allows the rapid investigation of new classes of narcotics.

Emission spectroscopy and absorption spectroscopy are closely related and instrumentation for both is quite often found in the same laboratory. Before discussing the specific application of ultraviolet absorption spectra to narcotic analysis, one should first know of the origin of absorption spectra, become familiar with the general components of the instruments used for measuring absorption spectra and understand the laws governing the attenuation of radiant energy passing through a homogeneous, isotropic, non-metallic medium.

2. Origin of absorption spectra

Emission spectra consist of sharp discrete lines arising from the transition of electrons from a term level of higher energy to a term level of lower energy in an atom or ion. These term levels can be defined by a principle quantum number, n; an azimuthal quantum number, l; a spin quantum number, s; and the resultant angular momentum, j. The term levels of molecules are designated by a similar system of symbols where Λ is analogous to the azimuthal quantum number, Σ the spin quantum number, and Ω is similar to the resultant angular momentum. In emission spectroscopy the electrons are pushed or "excited" to the higher energy levels by energy supplied by means of electrical discharge. The amount of energy absorbed in this process

is small and is not normally measured, since it is the energy emitted by the excited atoms which serves to qualitatively identify the atoms and to serve for their quantitative estimation. An application of emission spectrography in the narcotic analysis for the determination of countries of origin of opium samples by means of the composition of the opium ash has recently been made by Bartlet and Farmilo (1).

Absorption spectroscopy is a means of investigating narcotics by the energy absorbed in raising the narcotic molecule to excited states. While atoms and ions also demonstrate a similar property of energy absorption, it is more generally utilized in the determination of molecules, or particular groups of atoms in a molecule. The molecule is made up of several atoms and its total energy is the sum of the translational energy of the entire system, the vibrational energy, the rotational energy and the electronic energy of its components. Consequently, the energy terms for molecules are more complicated than for atoms; each spectral line of the atomic emission spectrum is replaced by a system of bands for the molecular absorption spectrum. (Two examples of atomic emission spectra and molecular band spectra are given in figures 2 and 13). Energy transitions which involve change of rotational energy alone involve relatively small amounts of energy and correspond to bands in the extreme infrared or microwave regions. (The origin of these spectra are discussed in part IV A of this series.) The vibrational energies are larger, so that changes in vibrational (and rotational) energy lead to bands in the near infrared. Transitions involving electronic rearrangements in molecules may lead to absorption in any region of the spectrum. The systems used in analytical spectrophotometry absorb energy between 2,000 Å (200 mμ) and 10,000 Å (1,000 mμ). In general the region of the spectrum in which an absorption band occurs is determined by the electronic transition, the gross structure of the system depends on the vibrational energy changes, and the fine-line structure of the individual bands depends on the rotational energy changes.

3. Instrumentation

Since qualitative spectrophotometry involves measurement of the energy absorbed by a sample as a function of the wave-length, and quantitative determinations depend upon measurements of the absorbed energy at a fixed wave-length, a spectrophotometer must consist of three essential components. These parts are a source of radiant energy, a means of dispersing the energy according to its frequency, a mechanism for detecting and estimating the amount of energy passing through the sample. In the diagram (figure 1) entitled "How a spectrophotometer works" these parts and their relation to one another can be seen from left to right in the diagram. (3) See figure 1.

In the ultraviolet and visible portions of the electromagnetic spectrum, three types of sources of radiation are normally used. For the ultraviolet region from 200-400 mμ, the continuum produced by a hydrogen discharge has been widely used (Lawrence and Edlefson, 1930, and Kistiakowsky, 1931). This source gives a continuous supply of radiation below about 350 mμ, and is readily adaptable for use with instruments that contain phototubes or photomultiplier tubes as radiation detectors.

Such sources are operated at hydrogen pressures ranging from 1 to 10 millimeters of mercury, at applied voltages from 3,000 to 5,000 volts, and at a fraction of an ampere to several amperes. A hot cathode, hydrogen discharge tube has been described by Allen and Franklin, 1939, 1941, (4) which operates at 80 volts and about 1.3 amperes. A ribbon filament incandescent lamp operating at a colour temperature of 2,400 to 2,800 degrees K gives a continuous source of radiation which may be used down to about 320 millimicrons. This limit is imposed by the glass envelope surrounding the filament.

A condensed spark between tungsten-steel electrodes is the most widely used source in photographic absorption spectrophotometry. This was the source employed for making all the benzene spectra illustrated in figure 2. In figure 2, the high intensity of the ultraviolet emission, the richness of the lines, and their fairly even distribution over the entire spectral range, freedom from wandering, and the localization of the luminous area in a small region may be seen. It is for these reasons that the tungsten-steel spark is preferred for work in the ultraviolet. The discontinuous character of the spectrum and the wide range of intensities between the strong and weak lines are disadvantages of this source. These two properties make the spectral image unsuitable for the detection of fine structure in absorption bands. The graph in the lower right hand corner of figure 2 was constructed from the spark-absorption spectra shown in the upper right hand corner. The graph in the lower left hand corner was constructed using a modern recording ultraviolet absorption spectrophotometer having as radiant energy source, a continuous discharge source.

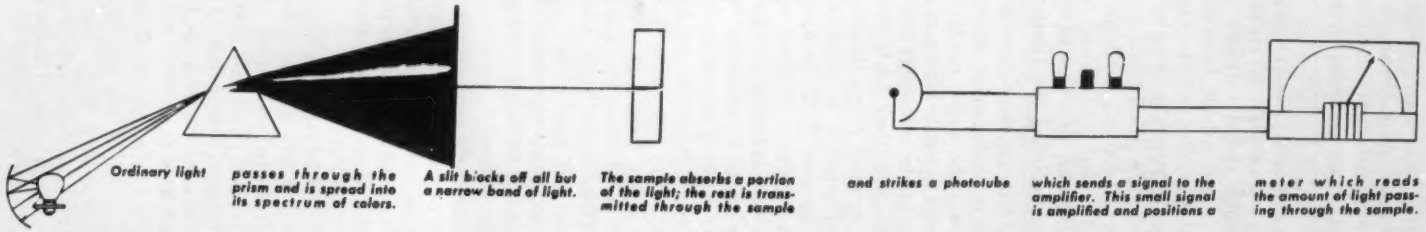
Spectral dispersion and isolation in the region between 200 and 1,000 millimicrons may be obtained by means of refraction through a prism; by the diffraction and interference associated with a fine line grating, or the spectral isolation may be effected by means of optical filters, there being no dispersing system in the ordinary sense.

Glass or quartz prisms of 60 degrees refracting angle, or equivalent prisms have been widely used in prism spectrophotometers for the ultraviolet and visible regions. Recently a spectrophotometer (Beckman model B) has become available which uses a Féry prism (3). Some instruments have been designed with a double prism monochromator to reduce stray light.

Gratings have been used to obtain dispersion of the radiant energy, with both transmission and reflection types being of value. A transmission grating, double monochromator spectrophotometer is claimed to have an average stray radiation of one per cent or less. However, in general, a grating monochromator has a higher relative intensity of stray radiation than a prism dispersing system. Cary and Beckman, 1941 (5), described a prism

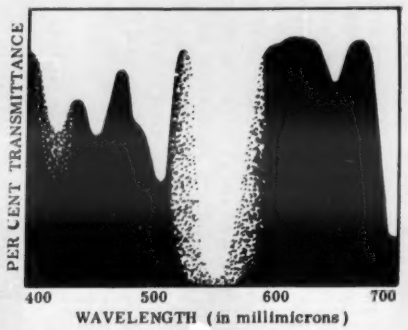
FIGURE 1

HOW A SPECTROPHOTOMETER WORKS


Ordinary light
passes through the prism and is spread into its spectrum of colors.
A slit blocks off all but a narrow band of light.
The sample absorbs a portion of the light; the rest is transmitted through the sample
and strikes a phototube
which sends a signal to the amplifier. This small signal is amplified and positions a meter which reads the amount of light passing through the sample.

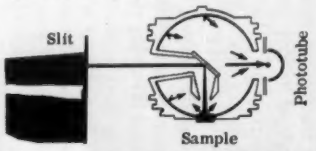
For visible light, a regular light bulb is used. Ultraviolet and infrared require special radiation sources. A large number of all measurements are made in the ultraviolet and the infrared regions of the spectrum. The desired color (wavelength) is selected by a knob which rotates the prism, causing the spectrum to move along the slit so that a different band of color falls on the slit opening and reaches the sample. The slit width is adjustable, allowing any band width of color to be chosen. The slits can be made extremely narrow to give high "resolution"—an important performance feature of a Spectrophotometer. Some of the light rays which enter the sample displace atoms from their normal position in a molecule and make them vibrate. The wavelengths which cause this vibration are absorbed by the sample. Light passing through the sample strikes the phototube where it is changed into an extremely small electric signal. The signal is then sent to an amplifier, similar to the one in an ordinary radio. By greatly increasing the strength of the minute signal from the phototube, the amplifier eliminates the need for delicate parts, permitting an instrument design which is resistant to shock and vibrations. The amplified signal positions the needle of an accurate meter to read the exact amount of light passing through the sample. The meter scale can be read directly in either transmittance or absorbance units.

Transmission (Absorption) Measurements. The drawing above shows how the Spectrophotometer measures the amount of a particular color (wavelength) of light absorbed or transmitted by the sample substance. By making a series of such measurements and using different wavelengths of light, the analyst can draw a curve as in Spectrum 1 which shows the exact location and degree of the absorptions of the sample over a wide range of wavelengths. This curve is the "absorption spectrum" . . . the unmistakable "fingerprint" of the sample.

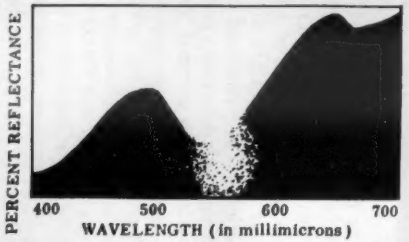


Spectrum 1. The Absorption Spectrum: The sample's molecular "fingerprint"

Reflection Measurements. The narrow band of color passing through the slit enters the Reflectance Attachment (below) and is directed downward onto the opaque, colored sample. The sample absorbs some of the light. The rest of the light is reflected, strikes the phototube and is registered on the meter. The "reflectance curve" (Spectrum 2 below) is the result of a series of such measurements made at different wavelengths. It is the only true picture of a color.

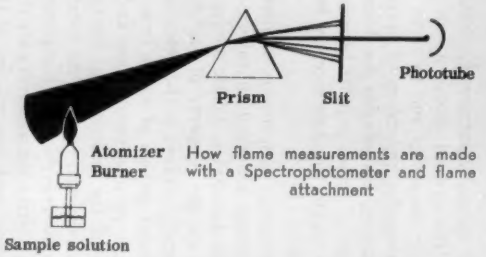


How reflectance measurements are made with a Spectrophotometer and reflectance attachment.

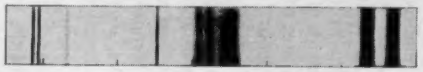


SPECTRUM 2. Reflectance curve of a salmon-colored building tile.

Flame Measurements. The sample, in liquid form, is atomized into a hot flame, as illustrated below, which acts as the light source for the Spectrophotometer. This flame excites atoms in the sample, causing them to emit radiations at various wavelengths (See Spectrum 3). By measuring these emissions, the Spectrophotometer enables unknown elements to be identified and amounts of known elements to be determined. Called "flame photometry", this method is extremely rapid (as fast as 10 seconds a measurement) and to date has been applied to over 50 elements and 700 substances.



How flame measurements are made with a Spectrophotometer and flame attachment



SPECTRUM 3. Emission of calcium when excited in a hot flame.

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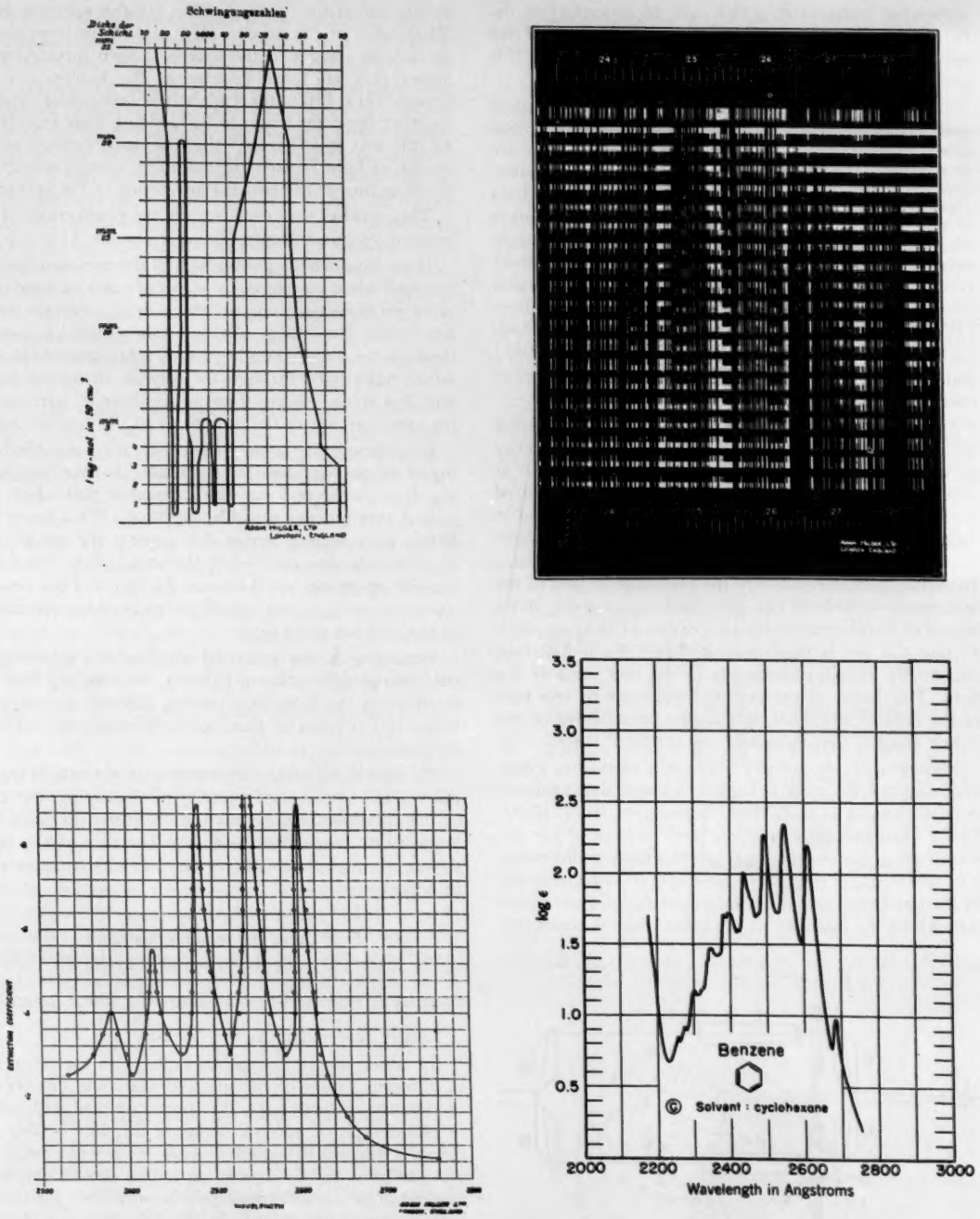


FIGURE 2

Historical development of methods of recording spectra. Absorption spectra of benzene. Upper left. *Benzene absorption spectra, according to W. N. Hartley, 1880, by method of relative thicknesses.* Upper right. *Photographic record of absorption spectra made on a Hilger spectrophotometer with tungsten steel arc, and conventional spectrograph, from Lothian.* Lower left. *Line graph constructed from the photograph* upper right *from Lothian, 1950.* Lower right. *Benzene spectra produced by the Cary recording spectrophotometer by permission John Wiley & Sons and Friedel and Orchin*

dispersing instrument, which will be described in detail later, since it is the instrument on which all the spectra of narcotics described in part III B of this series were obtained.

In certain kinds of work where it has been found sufficient to isolate only certain spectral regions, optical filters have proved to be satisfactory. These filters are of three types: (1) glasses, usually two or more in combination; (2) two or more dyes incorporated into gelatin or other media; and (3) interference filters. Information on the filtering characteristics of these filtering media may be obtained from the Corning Glass Works (6) (Glass Colour Filters (1946)), the Eastman Kodak Company (7) supplying the Wratten dye-gelatin filters (Wratten Light Filters, 1948), and the Farrand Optical Company (8) (Farrand Interference Filters, 1947) and Baird Associates (9) (Baird Associates Interference Filters, 1946) supplying interference filters.

Spectrophotometry consists essentially of measuring the ratio of two radiant energies at a specified frequency or wavelength, and then repeating this measurement at other frequencies or wavelengths as often as desired over the spectral range of interest. This is illustrated in figure 1. This ratio of radiant energies may be determined by visual, photographic, or photoelectric means. In visual spectrophotometry the photometric part of the instrument includes a two-part photometric field, and a means of varying the luminance of one of the two parts, so that the eye is used only to detect the unmatched, and finally to judge the match of the two parts of the field. The means of varying the luminance of one part of the field is calibrated, so that the actual value of the match point is determined by an auxiliary system.

Photographic photometry is normally used when a conventional spectrograph is used as a dispersing medium. A device known as a Spekker Photometer (10) (Hilger, 1937) illustrated in figure 3 is used in front of the entrance slit of the conventional spectrograph to illuminate it by two beams of light at the same origin A, the intensity of the one being varied by the absorbing medium under test, whilst the intensity of the other beam is controlled

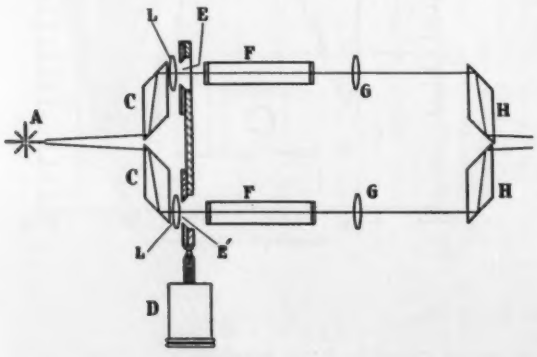


FIGURE 3

The Spekker Photometer, taken from Lothian by permission of Hilger & Watts, London, England

by the size of the opening of the variable aperture (E'). The angles of the prisms (H) (H') have been chosen so that the images of the source of light formed by the lenses (G) (G') are bisected at the junctions of the prisms (H) (H'), the two halves being thus brought together for comparison to be made of their intensities. In this way it is ensured that the same portion of the source of light is used for making a comparison at the dividing line of the two narrow bands of the spectrum.

This spekker was used to take the photograph of the benzene spectra in figure 2 (see reference 11).

If we consider the photograph of the emission spectra, we shall see it consists of a series of pairs of spectra in close juxtaposition, one of which is of a certain intensity, while the other, namely, that which has passed through the material under test, is more dense than that which has passed through the solvent, in certain parts, and less so in others, there being definite portions of the spectrum where the intensities of the two are equal.

Considering the points of equality, the equal blackening of the photographic plate indicates that the light passing through the test material is equal to that which has passed through the variable aperture (E') (figure 2). When no absorbing material is present the spectra are of equal intensity only when the areas of the fixed and variable apertures are the same, the ratios of the respective areas being a measure of the ratio of the intensities of the two beams of light.

Returning to the points of equality of blackening of the photographic plate in figure 1, one can say that the intensity of the light after passing through the medium under test is equal to that passing through the variable aperture.

The apertures' areas are proportional to the light transmitted, and at points of equality of blackening, the area of the variable aperture has been adjusted to make the intensity of the control beam equal to that of the light passing through the medium; the ratio of intensities may be represented by

$$\frac{Io}{I} = \frac{\text{Area of fixed aperture}}{\text{Area of variable aperture.}}$$

The drum (D) (figure 3) which controls the variable aperture is engraved to read $\text{Log}\frac{Io}{I}$, which logarithm is usually referred to as the "density".

By taking a series of photographs with the drum set to different values of density and searching out points of equality of the two spectra (points marked with a dot in photograph of spectra in figure 2), one is able to obtain a number of values of Io/I for a wide range of wave-lengths, and by connecting up the dots so obtained one can draw a graph connecting density (i.e., log Io/I) with the wave-length of light. These values are plotted as extinction coefficient (optical density) on the graph lower right hand corner figure 2. Because of the higher dispersion normally associated with spectrographs more fine structure may be investigated by this technique than can be observed visually or with photoelectric photometers.

Photoelectric detectors are of three types: (1) barrier layer cells (figure 4); (2) phototubes; and (3) photomultiplier tubes (figures 5 and 5a). A barrier layer cell (12) consists essentially of a plate of either copper or iron upon which a semi-conducting layer of cuprous oxide or selenium has been grown. The semi-conducting layer has been covered with a light transparent layer of gold, platinum, copper, or lead which acts as an electron collector. The average cell has an output of about 120 microamperes *per lumen* and can be used in conjunction with electrical indicators such as micro or milliammeters to detect and measure high levels of illumination. No external potential source is required with a barrier layer cell. Vacuum phototubes (12) require a source of potential illustrated in figures 5 and 5a and are normally used with a vacuum tube amplifier as shown in figure 7.

Over the range of intensities of radiation encountered in spectrophotometry the photocell is designed to give a linear response. Radiant energy comprised of photons dislodges electrons from atoms in the cell surface, which are drawn away from the surface by an electric potential producing a continuous electric current. The number of electrons which leave the surface is dependent on the amount of radiation falling upon it; the greater the number of electrons which come out of the surface the greater is the current produced. All photometers are designed on the basis of the linearity of this photoelectric response. For a linear photocell, R=Kα I, where R=instrument reading, I=intensity, and Kα=constant. Then Ro=Kα Io and $\log^{10} \frac{Ro}{R} = \log_{10} \frac{K\alpha\ Io}{K\alpha\ I}$ true absorbence. Not all photocells are linear in response to radiation according to Cannon and Butterworth (1953). A non linear spectrophotometer, although giving a linear Beer's law plot, will give erroneous values for absorptivity.

A vacuum tube of a special kind employing several electrodes or dynodes which achieves the equivalence of amplification within the tube itself is called a photomultiplier tube. These tubes have a higher signal-to-noise ratio than the phototube amplifier combination. The IP28 multiplier phototube (figure 5a) is capable of multiplying feeble photoelectric current produced at the cathode by an average value of 1,000,000 times when operated at 100 volts per stage. The output current of the IP28 is a linear function of the exciting energy under normal operating conditions.

4. The Beckman spectrophotometer (13)

The Beckman spectrophotometer is the instrument currently most often used in North America for measurement of absorption spectra. It is designed to operate in the ultraviolet, visible, and with some mechanical adjustments in the near infrared regions. A description of its three main parts, monochromator, photometer, and amplifier, will indicate how the spectrophotometer works.

The Monochromator

The optics of the Beckman spectrophotometer are shown in figure 6. One of the two interchangeable radia-

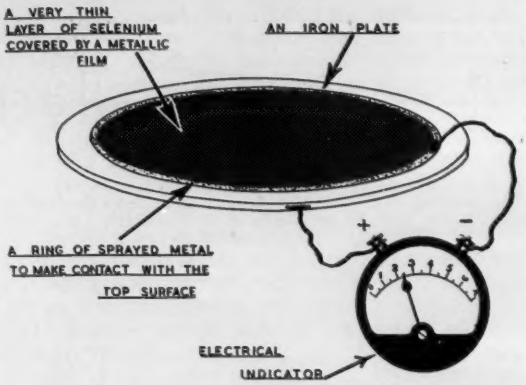

A VERY THIN LAYER OF SELENIUM COVERED BY A METALLIC FILM
AN IRON PLATE
A RING OF SPRAYED METAL TO MAKE CONTACT WITH THE TOP SURFACE
+
−
ELECTRICAL INDICATOR

FIGURE 4

The Barrier Layer Photocell, from the publication Electric Eyes, *by permission of the Tintometer Ltd., Salisbury, England*

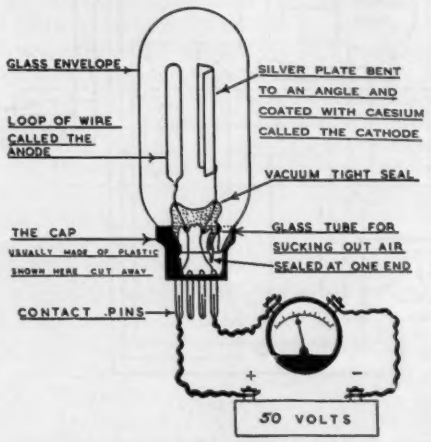

GLASS ENVELOPE
SILVER PLATE BENT TO AN ANGLE AND COATED WITH CAESIUM CALLED THE CATHODE
LOOP OF WIRE CALLED THE ANODE
VACUUM TIGHT SEAL
THE CAP
USUALLY MADE OF PLASTIC SHOWN HERE CUT AWAY
GLASS TUBE FOR SUCKING OUT AIR SEALED AT ONE END
CONTACT PINS
+
−
50 VOLTS

FIGURE 5

The Phototube, from the publication Electric Eyes, *by permission of the Tintometer Ltd., Salisbury, England*

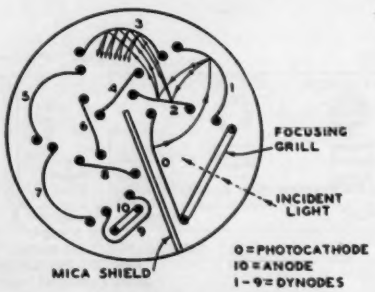


FIGURE 5a

The Multiplier Phototube

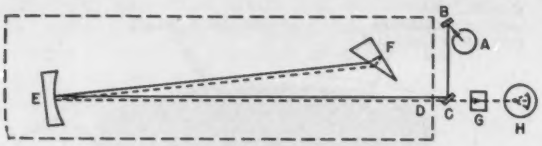


FIGURE 6

The optics of the Beckman spectrophotometer from the publication Electric Eyes, *by permission of the Tintometer Ltd., Salisbury, England*

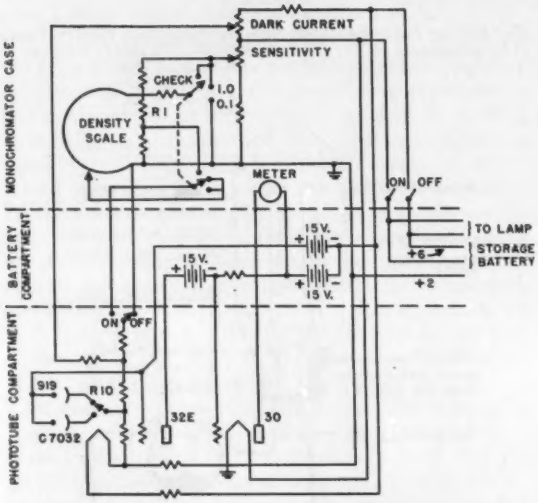


FIGURE 7

The wiring diagram of the Beckman phototube amplifier, from Kirk

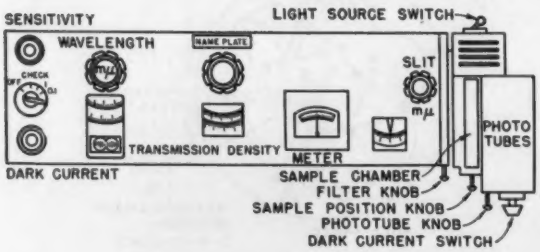


FIGURE 8

The control panel of the Beckman spectrophotometer, from Kirk

tion sources is used at A, depending on the *spectral* range desired. A standard 32-cp. prefocused tungsten lamp, (Mazda 2331) is used for the spectral region from 320 to 2,000 mμ. A special hydrogen discharge tube is used for the spectral region from 200 to 320 mμ. A 6-V. heavy-duty storage battery serves as the power source for the former. A new development which is useful when contemplating continuous use of the instrument over a long period is the Beckman D.U. power charger. This accessory has a space for the 6-V. battery and also locates the C batteries outside of the monochromator case. A special power unit or "powerpack" (as it is sometimes called) operates the hydrogen discharge tube. The two sources are mounted in a single housing on separate backs for ready changeover. A mercury discharge tube is also available to check the wave-length setting of a number of known wave-lengths.

Radiation from source A is magnified by the collimating mirror B, and the diagonal mirror C, and is focused on the plane of the slit at D. After passing through the slit opening, the radiation is reflected by the collimating mirror, E, onto the prism, F. The back surface of the prism is an aluminized mirror, and the radiation is reflected by this mirror, back through the prism and the mirror E to the slit D.

The internal optics, mirror E, and prism F, are so arranged that the emergent beam is approximately half an inch above the entering beam at the slit, D. The emergent beam then passes through the absorption cell in the cell holder, G and into the photocell, H.

The quartz prism, F, was selected as the light dispersion (splitting) device because it gives a spectrum relatively free of scattered light. The half prism, F, and reflecting mirror, E, not only require less quartz than a full prism but also obviate several complications which would arise if a full prism were used. Likewise, the use of collimating mirrors avoids the necessity of quartz lenses for focusing the radiation.

Variation in wave-length of the radiation is obtained by rotating the prism with a simple mechanical device. The wave-length setting can be varied slightly by moving the position of the collimating mirror, E; in actual practice this is only used in making initial adjustments.

The Photometer

The output (voltage) of the photocells is amplified by an electronic amplifier whose circuit is shown in figure 7. The essential feature of the circuit is that the phototube current is measured by balancing the voltage drop in the 2,000-megohm resistor (R10) with the slide wire potentiometer (R1). The indicating device is a sensitive milliammeter. The remaining controls are included to correct for stray currents in the amplifying circuit, and to adjust the circuit so that the percentage transmission and/or absorbence is read. The absorbence A (sometimes called optical density) is also read directly on the same scale as the transmission.

Control panel

The various knobs and dials on the instrument are shown diagrammatically in figure 8. The wave-length

knob controls the wave-length of the radiation passing through the cell holder (solution) and to the photocell. The wave-length scale indicates the radiation wave-length being isolated. The scale is not evenly divided and at one end (250-300 mμ) the scale divisions appear closely crowded together. The per cent transmittance (or absorbence) knob and scale are used respectively to balance the meter when a measurement is being made, and to indicate the percentage transmission and absorbence reading. Two scales are available, the upper being percentage transmission; the lower scale being absorbence (previously called optical density). For narcotic identification work the absorbence scale is used; for routine quantitative work the transmittance scale is often preferred. There appears to be a greater tendency to use absorbence values in all recent work. The third of the large control knobs adjusts the width of the slits.

The amplifier system of the spectrophotometer and the measurement of the absorption or transmission of an object requires that the output of the photocell when amplified gives a constant current. Since the outputs both of the source and the phototube vary with the wavelength of the radiant energy, some device must be inserted into the circuit to control either the output of the source, or the photocell, or both. In the Beckman instrument, both outputs are controlled. The slits at D in figure 6, operated by the third big knob on the panel, control mechanically the output of source A. A rheostat marked sensitivity varies the output of the phototube electrically. In practice, the two adjustments are used together, the slit width (large knob 3) being a rough adjustment, and the sensitivity rheostat a fine adjustment.

In addition to increasing the amount of radiation reaching the phototube, increasing the slit width widens the dispersion range of the radiation. This dispersion range should be kept as small as possible for accurate work; the slit width should be kept as low as possible. The dial setting is usually between 0.01 and 0.06 mm. for quantitative analytical work. (In practice, when obtaining a point by point description of the spectral curve the slit width setting varies with each wave-length, being wider for wave-lengths where radiation intensity is low; the slit widths therefore may vary from 0.06 mm. to 2 mm.)

The ammeter between the transmission and slit width knobs serves only to indicate a zero or "null" point, and the several divisions on either side are for convenience only. Throughout the various adjustments of the instrument, the object is to keep the needle at the zeropoint (i.e., constant current).

On the extreme left end of the instrument are two resistances and the main switch. The dark current resistance balances out any stray current in the amplifier. The sensitivity control is a potentiometer with a 9-turn helical winding and is essentially a fine adjustment whose purpose is the same as the slit adjustment, i.e., to control the output of the photocell by reducing the current electrically. The instrument should be operated with this control approximately from one to four turns from its most counter-clockwise position, which is its most sensitive range. Operation at the other end of the sensitivity scale, i.e., the clockwise end, requires a wider slit opening, and makes the response to the ammeter extremely sensitive to changes in the position of the transmission-absorbence knob.

The main switch has three "on" positions marked "Check", "1", and "0.1". The "1" position is the true "on" position. The "check" position is used when it is desired to adjust the meter against the blank. It avoids the necessity for returning the absorbence to zero, or transmission scale to 100, before each measurement. For readings greater than an absorbence of 1 (or less than 10 per cent transmission), the switch is turned to the "0.1" position, and the meter is balanced in the usual manner. The observed transmission scale reading is then divided by ten to give the true transmission. The absorbence reading is also changed. The value 1 is added to the observed absorbence reading. This permits a more accurate measurement on the scale in the region below an absorbence of 1.

On the right hand end of the instrument are three push-pull knobs and a switch. The first of the three knobs controls a filter which is necessary when measurements are made below 400 mμ with the tungsten light source. When the knob is in as far as possible, there is no filter in the light path. With the knob pulled out into the next position, a purple filter is introduced into the light path. This cuts off stray radiation which may enter the monochromator when the above combination of source and wave-length is used. The third and last position is blank.

The second knob (at the right hand end) controls the position of the absorption cells in the cell holder. This obviates the necessity of opening the cell container while a series of measurements is being made.

The third knob is a switch which selects the phototube and automatically makes the necessary circuit changes. No one phototube can cover the entire spectral range of the Beckman instrument. Two tubes are employed which are interchanged merely by pushing the phototube knob. When the knob is furthest out, the ultraviolet sensitive tube is in position, and all measurements below 620 mμ should be made with this phototube. For measurements between 620 and 2,000 mμ, the red sensitive tube is put in position by pushing the phototube knob in as far as possible.

The off-position of the "off-on" switch shuts off the photocell both optically and electrically from the remainder of the instrument. It is put in the off-position only when the dark current is being checked.

Table I

COMBINATIONS OF FILTER, PHOTOTUBE AND SOURCE IN OPERATING THE BECKMAN SPECTROPHOTOMETER

Spectral regions, mμ	*Filter control*	*Phototube control*	*Source*
220-320	In	Out	Hydrogen
320-400	Out	Out	Tungsten
400-620	In	Out	Tungsten
620-2,000	In	In	Tungsten

5. Spectrophotometric identification

Qualitative absorption spectrophotometry may be achieved by comparing the absorption curve of the unknown drug with curves of known compounds. Accurate data on the absorption of a sample as a function of wavelength must be obtained over a considerable portion of the spectrum to allow this method to be used. Similar structures within different molecules will show similar absorptions and likewise, very similar complex organic molecules will show very similar absorption spectra. In fact this generalization is so well established that tables of the wave-lengths of the absorptions of different groups in the ultraviolet and visible regions have been made (14) (see Harrison, Lord and Loofbourow, 1948).

Unfortunately no single comprehensive compilation of absorption spectra exists; some data have been compiled by the American Petroleum Institute Research Project 44 at the National Bureau of Standards. International Critical Tables (15) contains both absorption data and references to literature containing spectra of both organic and inorganic compounds. *Tables annuelles de constantes et données numériques, données numériques de spectroscopie,* vols. I to XII by V. Henri and L. Bruninghaus (16) contain tabulations of absorption data. Literature references to absorption are contained in *Physikalische Chemische Tabellen,* edited by Roth and Scheel (17); *Handbuch der Organischen Chemie,* fourth edition by Beilstein (18); and *Handbuch der Inorganischen Chemie,* eighth edition by Gmelin (19).*

Sources of information including books, review articles, miscellaneous articles, instrumentation and technique, and manufacturers, were collected by Hirt (1952) (20). Hirt is also in charge of a project for the publication of UV spectra. A recent atlas of ultraviolet spectra of aromatic compounds was written by Friedel and Orchin (1951) (21). Since no critical survey of the literature of absorption spectrometry has been made with respect to narcotics, a more or less complete historical review of ultraviolet absorption spectrophotometry related to narcotic analysis is included in the next section.

6. Historical review of ultraviolet absorption spectrophotometry related to narcotic analysis

The earliest reference (22) to the study of ultraviolet spectra is by Brewster (1833) although Miller (23) and Stokes (1852) appear to have done the first serious work (24). Sir William Noel Hartley (1881), Chemistry Professor, Royal College of Science, Dublin, using Miller's original quartz spectrograph (23) reported the first ultraviolet spectra of narcotics, and he appears also to have been the first to suggest the use of these spectra as evidence in alkaloid identification in court cases. In a report (25) to the Royal Society of London, Dec. 1884, Hartley described the results of measurements and illustrated by means of graphs the spectra of thirty-two alkaloids, including the following opium bases and their derivatives: morphine, narcotine, codeine, thebaine, papaverine, oxynarcotine, apomorphine hydrochloride, cotarnine hydrobromide, diacetylmorphine and acetylcodeine.[1] Keeping in mind the relative knowledge of the time, the comments of Hartley are interesting. The difficulty of identifying these alkaloids by distinctive chemical reactions and their physiological action was pointed out by Hartley. "The facts", he stated in 1884, "are well known, and are generally made use of by counsel for the defence in medico-legal cases. . . ." and further as an example, Hartley states that "The evidence given at the trial of George Henry Lamson, a surgeon, at the Central Court in 1882, for poisoning with aconitine, conferred greatly increased importance upon any method of absolute physical measurement which might be substituted for the ordinary tests in the identification of the dangerous alkaloids. Almost all alkaloids have a complex chemical constitution, and every complex molecule in which carbon is in a certain state of condensation has a definite absorption spectrum in the ultraviolet if not in the visible region. In most cases the absorption curve is peculiar and often strikingly characteristic, and only minute quantities of material are actually required for obtaining measurements of spectra from which such curves may be plotted. The interest that attaches to an examination of the absorption spectra of the alkaloids is not alone the fact that a means of recognizing, detecting, and estimating such substances may be devised, but still more, that we may learn something of their chemical constitution."

Hartley's conclusions (1884) also showed his main interest to be in structure determinations, for he indicated that morphine, codeine, and their derivatives apomorphine hydrochloride, mono-acetylmorphine, and diacetylmorphine,[2] all have a similar condensed nucleus. This nucleus Hartley believed was a benzene or pyridine derivative, since as he showed, the main absorption band extended from 2,600 Å to 3,000 Å. He showed, also, the effect of alkyl and acetyl substitutions, upon the curve of absorption as exemplified by codeine and the acetylated derivatives of codeine and morphine. Later in 1887 Hartley from these and other studies advanced the belief that the absorption spectra of derivatives are characteristic of the parent molecule of an organic substance and are merely altered by additional chromophores, auxochromes, or substituents (26).

Dobbie became a student of Hartley's in 1898 and did further work in measuring spectra, some of which were of narcotics. In 1903 Dobbie measured the spectra of cotarnine and a number of alkaloids (27) and discussed their molecular constitution in terms of spectra. Dobbie also measured the spectrum of papaverine. He used the tautomeric equilibrium reaction of cotarnine in basic solutions as an indicator of the strength of alkaline

* Project No. E13 of the American Society for Testing Materials for the compilation of spectral data includes IBM coding. Inquiries should be directed to Dr. R. C. Hirt (see reference 20) or Dr. George Buc, editor of *Applied Spectroscopy.*

[1] The last two were called tetraacetylmorphine and diacetylcodeine, at the time.

[2] Which he called diacetylmorphine and tetraacetylmorphine.

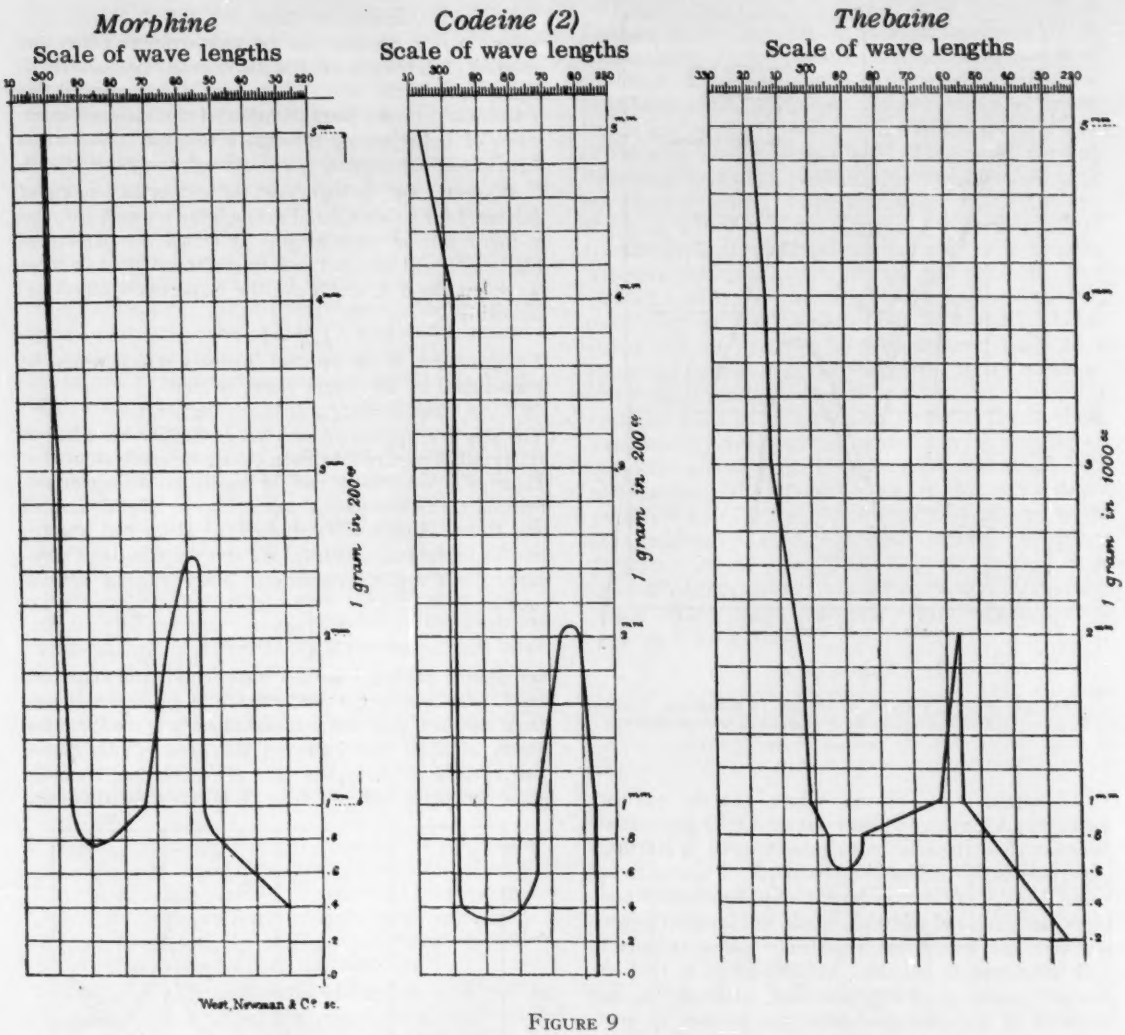


FIGURE 9

The line transmission of spectra of morphine, codeine, and thebaine, according to Hartley (1885)

hydroxides, and followed the course of reaction by means of ultraviolet spectrophotometry. In 1911 Dobbie showed the identity of the spectra of codeine and neopine (27); and in 1914 related the structure of a number of spectra of isoquinolines with that of papaverine.

Lothian (1937) critically evaluated this early work and made the following comments about it (11).

> "Unfortunately, much of the work done prior to about 1910 was valueless, since the methods employed were either entirely qualitative, or at best semi-quantitative, compared with those available today. Some uniformity was introduced however, by Hartley and other workers after him who developed a method in which the wave-lengths at which various thicknesses of a given solution ceased to transmit were recorded photographically" (see ordinate scales, figures 2, 9 and 13). "By diluting the solution progressively, the course of the absorption could be followed up to its maximum of intensity, and a curve of equivalent thicknesses of standard solution (or logarithms of these thicknesses) as ordinates against the observed limiting wave-lengths transmitted as abscissae then reproduced the main characteristics of the absorption band." (44)

The absorption spectra of morphine, codeine, and thebaine determined by this "equivalent thickness method" as recorded by Hartley (25) (figure 9) are compared with the same spectra shown in figure 10 which were obtained by a modern photometric method and plotted in terms of logarithm of the absorbence index. The location of maximum of absorption spectra by Hartley seem

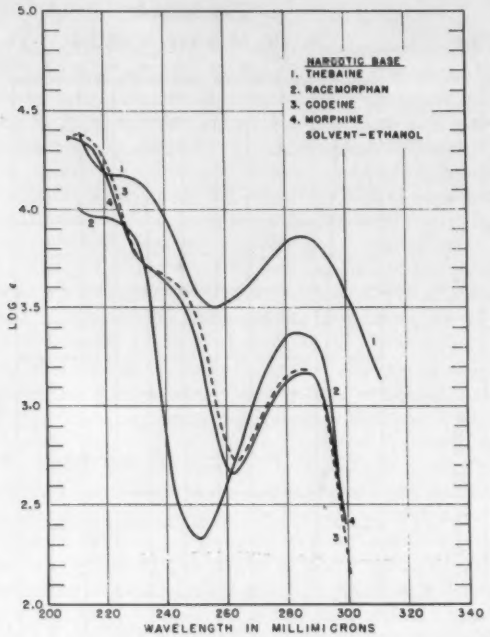


FIGURE 10

Comparison of line, absorption, spectra of morphine, codeine, thebaine, and racemorphan by a modern spectrophotometer

to be within 5 mμ of our values, but the intensity parameter determined by the equivalent thickness method does not show the relation to quantity used in Hartley's experiments and unless the conditions of measurement were identical, the curves for different substances, morphine, codeine, and thebaine, would not be strictly comparable. The use of the absorbence index (ϵ) makes such comparisons possible. Another point is that the detailed course of absorption (fine structure) is not recorded by the older method as can be seen by comparing the sequence of benzene absorption spectra (figure 2) recorded by Hartley (1883) and by Friedel and Orchin (1950) using a Cary recording spectrophotometer (21). This sequence indicates the historical development of ultraviolet spectra starting with the plotted record of perhaps the first practical quartz spectrograph (1885), through the photographic era with the Hilger Spekker ultraviolet photometer and medium quartz spectrograph (1910-1940) to the continuous 10 minute record of the Cary spectrophotometer (1950). The difference in fine structure and range may be seen in this comparison.

Henri (1913) (28) introduced a new concept into absorption spectrophotometry which enabled him to plot the intensity in terms of wave-length in a new way. Schwarzschild had discovered that the blackening of a photographic plate is related to the quantity of light falling on it by the expression

$$\text{density of blackening } \alpha\ I\ t^n$$

where n is a constant of the photographic plate, and method of development. I is the intensity or quantity of light, and t is the time of exposure. Henri applied this relationship to the determination of the ratio of intensities of light passing through a solution containing a light absorbing substance, and through the solvent itself.

If spectra are photographed through equal lengths of solvent, l for a time t_o; and through the solution for time t, there will be wave-lengths at which the density of blackening will be equal in each spectrum. Then at these wave-lengths if I_o and I are the respective transmitted intensities

$$I_o t_o^n = I\ t^n$$

I is that part of the incident intensity which would be transmitted by the solute alone, so that

$$\text{density} = \log_{10} Io/I = n\ \log_{10}(t/t_o)$$

The practical application of Henri's density wave-length relationship required the independent determination of n. Henri was the first to use the logarithm molecular extinction coefficient plotted against wave-length. Gompel and Henri (1913) (28) studied the ultraviolet absorption of morphine, codeine, and apomorphine and compared them with phenanthrene. They utilized the expression

$$\varepsilon = \log \frac{I\,o}{I}\ (\text{cm. mol.})$$

and plotted the log. ε against wave-length λ in angstrom units. This symbol ε, called extinction, probably derives from the fact that the measurements are made at the points of equal extinction on the photographic plate. The spectra of absorption for phenanthrene, apomorphine, morphine and codeine by Henri are shown in figure

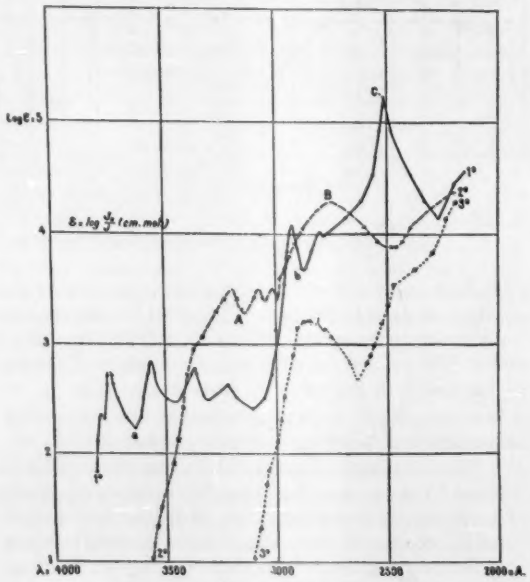


FIGURE 11

Spectrophotometric absorption of phenanthrene, apomorphine, morphine, and codeine, according to V. Henri (1913)

11). Henri's morphine (codeine) spectrum shows a maximum at 2,830 Å.

Henri (29) (51) (52) carried further the chromophore concept earlier stated by Hartley, i.e., that the absorption spectrum does not result from the action of the whole molecule on the incident radiation, but as a result of only particular parts of a molecule. For example, Henri showed that simple ketones exhibit an absorption band with an absorbence index of about 15 between 2,700-3,000 Å, acetone having a maximum at 2,800 Å. Using some examples from our own experience with narcotics it is observed that complex ketones like dihydrocodeinone, dihydromorphinone, dihydrocodeinone enol acetate, ketobemidone, methyldihydromorphinone all have an absorption maximum at about the same location as the acetone maximum, namely at 280-282 mμ. With the exception of ketobemidone they all have extinction coefficients (E=K C d) of about 1,200 to 1,250. Ketones belonging to the diarylalkoneamine group like amidone, isoamidone, pipidone and phenadoxone, all absorb between 292-296 mμ, at much lower intensities (about $\varepsilon = 500$). Henri's observations on such similar homologous series of ketones were: (1) that the absorption curves were similar in shape, that the main maximum moves toward longer wave-lengths and the intensity of the main band increases as the molecular weight increases. Henri found that other groups beside the carbonyl (C=O) behave in the same manner, in relation to their effect on the absorption spectra of the compound containing them. Thus Henri extended the chromophore concept to include groups other than those associated with visible colour which could give rise to a characteristic absorption in the ultraviolet region of the spectrum.

Henri and Zangger in 1912 discussed the application of ultraviolet spectra in the solution of problems of identification and detection in the field of forensic medicine (30). Zangger referred to the early application of the quartz spectrograph (Hilger) in the qualitative determination of alkaloids in this field (31).

Steiner (1922) studied the absorption spectra of isoquinoline alkaloids, especially papaverine and related spectra which he compared to veratrol (32). The values for papaverine base and hydrochloride Steiner obtained are compared with those obtained by us. Steiner's values are listed on the left and ours on the right. Values for papaverine hydrochloride were also given by Steiner. Narceine was found by Steiner to have a maximum at 2,707 Å and $\varepsilon = 9{,}800$; we have found the same compound to have the following values, λ max=2,700 Å and ε=9,620. Narcotine, hydrastine, opianic acid and hydrocotarnine were also studied by Steiner. The spectrum of narcotine was the result of contributions from opianic acid and hydrocotarnine mainly determined by the benzene chromophore present in opianic acid.

λ *max, Å*	ε *max*	λ *max, Å*	ε *max*
3,261	5,400	3,270	4,720
3,117	4,800	3,140	3,990
2,802	6,400	2,795	7,170
2,346	54,000	2,390	68,200

Hans Fischer (1925) a student of V. Henri and H. Zangger at the Institute of Forensic Medicine in the University of Zurich prepared a thesis which reviewed the history and application of spectrographic methods in general to identify alkaloids and compounds of toxicological interest (33). Fischer used a Hilger spectrograph, of the same kind employed by V. Henri, having a high dispersion power and yielding a spectrum measuring 27 cm. between the wave-lengths 2,200 to 3,200 Å with a precision of 0,0001 Å in this region. Fischer's opinion of the usefulness of spectrophotometry in forensic medicine was very enthusiastic. He believed that impurities play a minor role in spectrophotometric analysis. Comparing colour, crystal, and spectrophotometric tests, Fischer stated that the first two methods achieve results by a process of destruction, which in courts of law is not desirable; while spectrophotometry left the original molecule unchanged and at the same time identified the molecule. The same arguments are in vogue today by protagonists of the two schools; some recommend chemical tests, some physical tests. The answer probably is that both tests are extremely useful. A very practical demonstration of the interrelationship of physical and chemical methods is to be seen in the laboratories of the New York State Racing Commission (34), where upwards of 300 samples a day can be tested employing all three types of tests in each drug analysis.

The spectra of narcotics and derivatives studied by Fischer were: benzoylecgonine, opianic acid, meconin, ecgonine, cocaine, papaverine, narcotine, narceine, morphine, apomorphine, codeine, thebaine, and heroin. In figure 12 a set of spectral curves obtained by Fischer for

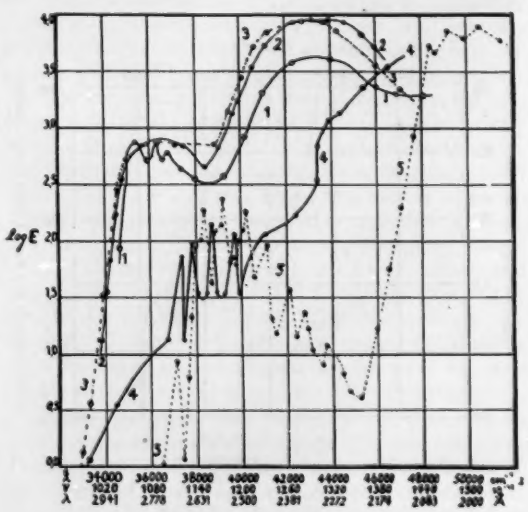


FIGURE 12

(1) Benzoic acid in hexane, (2) Benzoyl ecgonine in water, (3) Cocaine hydrochloride in water, (4) Tropic acid in alcohol, (5) Benzene in hexane. Absorption curves, according to Fischer (1925)

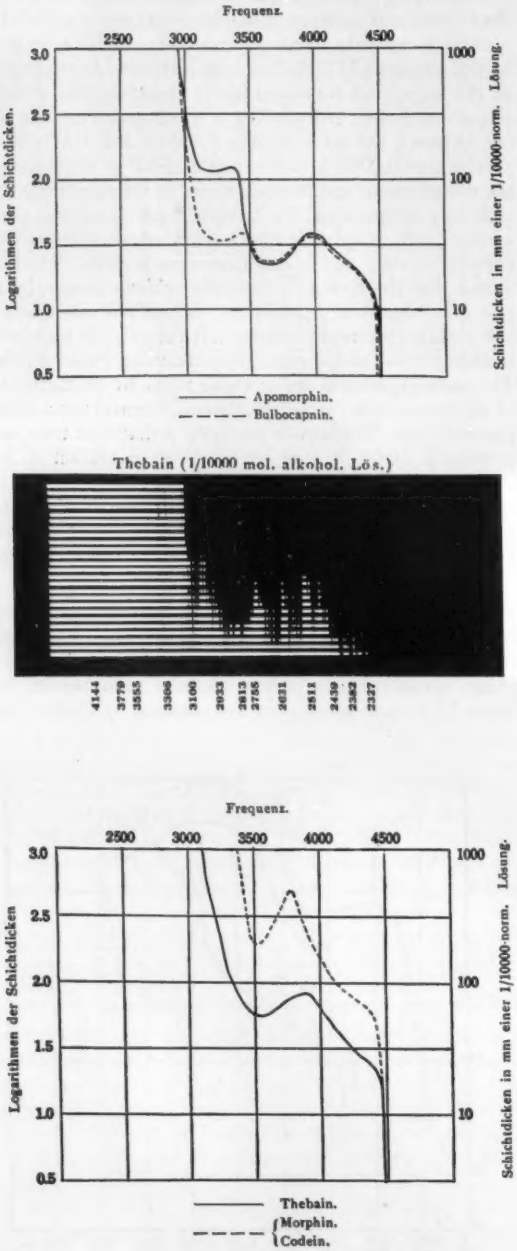


FIGURE 13

Spectra of opium alkaloids, according to Kitasato (1927)

benzoic acid, benzoylecgonine, and cocaine are given, along with those for tropic acid and benzene. The spectra are plotted as log. E against wave-length, Å, wave numbers, cm^{-1}, and frequency 10^{-12}. The similarity of the absorption curves for the first three compounds is striking.

Bontempi (1925) reported that morphine and morphine hydrochloride had the same spectra and concluded that hydrochloric acid had no effect on the spectrum of morphine (35). Eisenbrand (1926) reported that morphine could be determined in amounts as low as 0.2 mg by means of absorption spectra (36).

Brustier (1926) measured the line spectra of narcotine, morphine and ethylmorphine, and expressed these graphically (37).

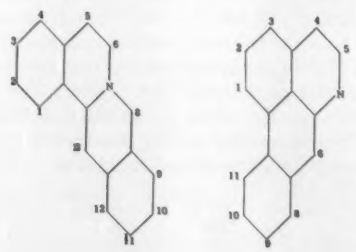
Kitasato (1927), using a Hilger quartz spectrograph, photographed the absorption spectra of 42 alkaloids (38). The curves and photograph in figure 13 illustrate Kitasato's method and results. Data from the photograph of spectra of 0.001 M solution of thebaine in alcohol was plotted as a transmission curve in the upper graph of figure 13. The logarithm of the thickness of the absorbing layer is plotted against the frequency cm^{-1}. The various corresponding relative layer thicknesses are also shown in mm. In the photograph the absorption maximum occurs between 2,813 and 2,933 angstroms. It should be remembered that this is a transmission type curve. The numbers shown as frequency are wave numbers, $\bar{\nu}$ mm^{-1}, where $\bar{\nu} = \frac{1}{\lambda}$ cm$=cm^{-1}$. For the morphine curve, the maximum absorption occurs at 3,500 mm^{-1}. The wave-length calculated to correspond to this frequency is

$$\lambda \text{ cm} = \frac{1}{35000} = 0.00002857 \text{ cm}$$

$$\lambda = 2857 \times 10^{-8} \text{ cm} = 2857 \text{ Å} = 285.7 \text{ m}\mu$$

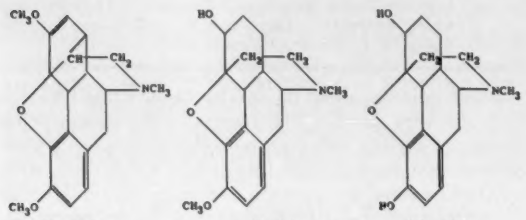
where 1 Å$=10^{-8}$cm. Hartley (1885) had determined the maximum wave-length to be 290 mμ according to the illustration in figure 9. Modern photometric determinations show a maximum at 285 mμ.

Kitasato classified the alkaloids into two major classes with the following basic structures (38):



I *II*

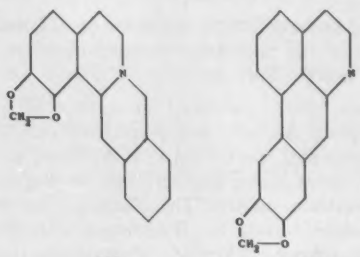
The following opium alkaloids were in class I, group III: cryptopine, protopine; group IV, narcotine, narceine; group V, papaverine, N-methyl-papaverine hydrochloride; group VI, cotarnine; the following alkaloids were in class II, group I, apomorphine; group II, thebaine; group III, morphine, codeine. The formulae used by Kitasato to represent thebaine, codeine and morphine, are as follows:



Thebaine *Codeine* *Morphine*

It is on this basis that Kitasato classified the alkaloids into the isoquinoline series. Thebaine according to Kitasato showed absorption at a "frequency" of $3{,}510^{cm.-1}$ (wave number) or 284.9 mμ and morphine and codeine were shown as having identical absorption curves and a maximum at $3{,}485^{mm.-1}$ (286.9). The hypsochromic absorption of the two latter alkaloids in comparison with thebaine is explained by the lesser number of double bonds and the auxochromic effect of the methoxyl and hydroxyl respectively. The great difference between the light absorption of thebaine compared with morphine or codeine and compared with apomorphine was noted by Kitasato and attributed to the difference in the type of nitrogen ring. Apomorphine ultraviolet spectra obtained by different Hilger instruments were shown to have fine structure between 300 and 325 mμ as found by Gompel and Henri (1912), and Elvidge (1940) (39). Recent determinations with the Beckman DU failed to detect the three small bands and showed a plateau in this region. Kitasato postulated that three ultraviolet characteristics could be explained since apomorphine has a pyridine ring connected to an aromatic nucleus while morphine has a pentamethylene-like structure connected to a hydrogenated ring as shown in the formula. The Gulland-Robinson structure is now generally accepted as the correct one for the series, and Kitasato's explanation has to be modified, in the light of modern theory.

Kitasato's study in the tetrahydroisoquinoline series showed that molecules containing a methylenedioxy or methoxy group have spectra with a single band at 3,200 Å for compounds with the auxochrome in the 1, 2 position and at 3,650 Å for compounds substituted in the 10, 11 position. Absence of 1, 2 substituents results in a flat curve at 3,200 Å while 9, 10 substitution instead of 10, 11 substitution has a bathochromic effect on the second band. Changes from tervalent (–N <) nitrogen to quinquivalent $(R_1R_2R_3\text{-}NH)^+$ nitrogen were observed to exert hyper and bathochromic effects in the two classes with the structures III and IV.



III *IV*

O. J. Walker (1939) reviewed the literature on absorption spectrophotometry for the period from 1932 to 1938 and provided a comprehensive list of references from a large number of scientific journals covering this period (40). The work on alkaloids and particularly narcotics was limited to 14 papers covering only alkaloids of the quinoline, ergot, strychnine, cinchona and berberine groups. Analytical, pharmacological and toxicological applications were described by V. Brustier (1932) and H. Fischer (1933) (41).

Elvidge (1940) investigated the possibility of application of spectrometric absorption methods in the routine control of pharmaceutical preparations such as tablets and ampoules of a number of alkaloidal drugs for which chemical methods of assay were not generally available or applicable (39). Absorption curves were given for the following narcotic and related alkaloids: morphine, diamorphine, codeine, codeine phosphate, and apomorphine hydrochloride; these were obtained in isopropyl alcohol and 0.5 N/HCl except for codeine. Morphine alkaloid was considerably altered in N/1 NaOH, a new absorption maximum occurred at 256 mμ in place of the usual inflexion (246 mμ) which appears in the salts and freebase in alcohols, and a bathochromic shift of the λ max 276 mμ to 296 mμ. These data may be of use in distinguishing morphine from other non-phenolic alkaloids of the same general structure. Apomorphine showed a curve characteristic from the rest of this series, and had pronounced absorption at 273 mμ together with fine structure from 300 to 325 mμ. This fine structure, Elvidge stated, would well serve as a means of identifying small quantities of this alkaloid. Recent work has been unable to confirm presence of the fine structure.

Cocaine was studied by Ellinger in 1937 and its absorption spectrum recorded in the *Tabulae Biologicae Periodicae* (vol. XVI) (42). Elvidge (1940) studied the spectra of cocaine and related cocaine substitutes as follows: hydrochlorides of cocaine, orthocaine, benzamine, amydricaine, phenocaine, amylocaine, procaine. The following four related structures give absorption curves of very similar shape: cocaine, amydricaine, amylocaine, benzamine. Water was used as a solvent in all cases, except with orthocaine, and in some cases the

differences obtained by using water and alcohol as solvents were noted. The extinction values were expressed as $E\ \frac{1\%}{1\ \text{cm.}}$, which expression is used when molecular weight is unknown. The influence of pH and solvent on shape of the ultraviolet absorption curves of these drugs is noted (39).

Csoskan (1942) published an account of spectra of twenty opium alkaloids and derivatives (43). He used a Zeiss chemical spectroscope, a Wolfram arc source, and a Winters silver grating; and photographed the comparison line spectra. The alkaloids for this work were obtained from S. Boehringer (Ingelheim-am-Rhein) and from E. Merck (Darmstadt). Double-distilled water and 96 per cent ethanol were used as solvents to make solutions of 0.001 molar concentration. The wave-lengths were recorded in millimicrons and log E values were plotted against wave-length to obtain the extinction curves.

Results showing maxima and log E values from Csoskan's work are tabulated in table III to compare with our findings. The curves in his publication were too small for practical use. Csoskan states that on account of the incompleteness of the experimental measurements the early work of Kitasato and Steiner can only serve for gross qualitative comparisons and that their maximum wave-lengths are in general agreement with his. In discussing the spectral curves of the opium alkaloids Csoskan grouped the opium alkaloids into two classes according to molecular skeleton as follows:

Table II

CSOSKAN'S CLASSIFICATION OF OPIUM ALKALOIDS AND SPECTRA

I. *Alkaloids with phenanthrene-isoquinoline skeletons*
   A. 1. Morphine, 2. Codeine, 3. Thebaine, 4. Neopine.
   B. 1. Apomorphine, 2. Morphothebaine, 3. Epiapomorphine.

II. *Alkaloids with the benzylisoquinoline skeletons*
   A. 1. Papaverine, 2. Narcotine, 3. Narceine, 4. Cotarnine and hydro-cotarnine, 5. Laudanine, 6. Laudanosine, 7. Cryptopine, 8. Protopine, 9. Gnoscopine.

Csoskan points out that the spectra of the Class IA alkaloids are very similar. The spectra of the apomorphine group are slightly different, morphothebaine being very different and having 3 band maxima. The alkaloids with a benzylisoquinoline skeleton are quite dissimilar, and the hydrastinin spectrum is similar to that of narcotine.

Salomon and Bina (1946) studied the ultraviolet spectrum of mescaline sulphate, the active component of the peyote cactus. These authors found an absorption range from 240-280 mμ with fine structure from 272-286 mμ (44).

Strait, Kumler, Sah, Alpen and Chang (1948) discussed the ultraviolet absorption spectra of isomeric amidones and their structure (45). They pointed out that the spectra are characterized by expected phenyl absorptions

Table III

SPECTROPHOTOMETRIC DATA OF OPIUM ALKALOIDS, ACCORDING TO CSOSKAN (43)

Substance	*Solvent*	*Band maxima*					
		log E	λ mμ	*log E*	λ mμ	*log E*	νmμ ν
Phenanthrene							
morphine HCl	H_2O	—	—	3.08	282	3.49	242
morphine HCl	C_2H_5OH	—	—	3.11	287	3.50	242
codeine HCl	H_2O	—	—	3.08	282	3.49	242
thebaine HCl	H_2O	—	—	3.24	283	3.68	230
apomorphine HCl	H_2O	2.83	310	3.48	275	3.26	236
apomorphine HCl	—	—	—	3.42	264	3.33	224
morphothebaine HCl	—	2.30	295	3.47	263	3.47	218
papaverine HCl	—	3.79	311	3.80	280	3.24	247
papaverine HCl	(Steiner)	3.82	305	3.82	284	4.76	238
veratrol	—	—	—	3.35	275	3.86	226
papaverine HCl	(synthetic)	3.86	332	3.94	284	4.76	234
papaverine	—	3.43	325	3.50	274	5.54	237
papaverine	(synthetic)	3.43	325	3.76	272	4.58	234
narcotine HCl	H_2O	—	—	3.46	310	3.21	280
narcotine HCl	C_2H_5OH	—	—	3.61	299	3.40	280
hydrastine HCl	H_2O	—	—	3.62	290	3.46	278
narceine HCl	H_2O	2.07	375	3.75	285	3.73	231
cotarnine HCl	H_2O	3.96	333	3.93	252	3.96	212
hydrocotarnine HCl	—	—	—	3.14	286	4.10	215
benzylethylamine	—	—	—	3.30	279	4.21	246

near 260 mμ and by anomolous absorbances near 300 mμ, and an unexpected strong band below 260 mμ in the spectrum of amidone and its nitrile in basic and hexane solutions in contrast with isoamidone and its nitrile. The differences (interchange of a methyl group between adjacent atoms) in the "accepted" structures of amidone and isoamidone and their nitriles are incompatible with these spectrum differences. They proposed that amidone has only *one* phenyl rather than the two "accepted" phenyl groups on the number four carbon atom to explain the spectrum characteristics. The spectrum character of isoamidone is compatible with the two "accepted" phenyl groups on the same carbon atom. They attributed the strong band below 260 mμ to the enol and enamine structures, thus possible only in amidone and its nitrile. The band at 290-300 mμ present in the amidones is associated with the α-phenyl carbonyl structure (Schultz, Robb and Sprague, 1947) (46).

Morgan (1949) and co-workers at the New York State Racing Commission Laboratory have applied ultraviolet spectrophotometry to a very large extent both qualitatively and quantitatively to determine many drugs extracted from urine and saliva samples from horses (47). The use of buffered drug solutions for measurement of ultraviolet spectra at different pH's has been made since at least 1949. They have utilized buffers instead of addition of acids. The buffers which are employed by Morgan *et al.* are listed in table IV.

St. John (1949) at Eli Lilly and Co. Laboratory in Indianapolis reported that a number of alkaloids including morphine were being analysed by ultraviolet absorption spectrophotometry (48).

Hubach and Jones (1950) described the use of ultraviolet spectra along with other optical properties, and microchemical reactions for identification of amidone hydrochloride. They listed maxima at 294 mμ, 259 mμ, and 292 mμ, having the following extinction coefficients: 460, 480, and 520.

Montesinos Ampuero (1951) studied the spectrophotometric determination of cocaine in solution by means of a Beckman spectrophotometer (50).

Foster and MacDonald (1951) described the ultraviolet spectral changes of papaverine at different pH's. They discovered that the position of the max. of the absorption band was very pH dependent (51). Papaverine hydrochloride behaves as a very sensitive indicator in the ultraviolet.

Shaw and Jefferies (1951) determined the spectrum of phenadoxone, λ max 259, $E\ \frac{1\%}{1\ cm} = 13.6$; 292, 14.2 in water and in alcohol at 260 mμ, 12.0, at 294.5, 11.8 using a "Uvspek" photometer, concentration 0.1 per cent w/v, 0.5 cm cell (52).

Stuckey (1952) reviewed the pharmaceutical analytical applications of ultraviolet absorption spectrophotometry from the period 1936 to 1952. In dealing with alkaloids, especially narcotics, mention is made of the work of Elvidge (*loc. cit.*) on cocaine alkaloids and of the effect of pH on the morphine alkaloids.

Table IV

BUFFER COMPOSITION AND ABSORBANCY, ACCORDING TO MORGAN (1949)

pH	*Amounts of M/5 solutions of buffer constituents in 100 ml. of buffer*	*Wave-length (millimicrons)*									
		220	*230*	*240*	*250*	*260*	*270*	*280*	*290*	*300*	*310*
1.1	{HCl, 47.3 ml. {KCl, 2.72 ml.	.011	.007	.004	.003	.003	.002	.001	.001	.002	.001
2.0	{HCl, 5.95 ml. {KCl, 44.1 ml.	.006	-.003	-.005	-.002	-.002	-.003	-.003	-.003	-.004	-.003
2.8	{KH_2PO_4, 25.0 ml. {HCl, 3.50 ml.	.004	.003	.003	.003	.005	.001	.002	.001	-.001	-.001
4.0	{KH_2PO_4, 25.0 ml. {HCl, 0.25 ml.	.004	.004	.001	.001	.002	.002	.001	.001	.000	.000
5.1	{KH_2PO_4, 25.0 ml. {NaOH, 0.25 ml.	.027	.024	.023	.023	.022	.015	.016	.014	.011	.010
5.8	{KH_2PO_4, 25.0 ml. {NaOH, 2.82 ml.	.039	.029	.021	.016	.015	.016	.015	.011	.010	.006
7.0	{KH_2PO_4, 25.0 ml. {NaOH, 14.8 ml.	.042	.030	.021	.018	.017	.015	.014	.011	.007	.004
7.9[a]	{H_3BO_3-KCl, 25.0 ml. {NaOH, 2.00 ml.	.076	.050	.032	.026	.023	.023	.023	.018	.013	.009
9.0[a]	{H_3BO_3-KCl, 25.0 ml. {NaOH, 10.7 ml.	.147	.105	.077	.067	.063	.058	.053	.045	.036	.030
10.0[a]	{H_3BO_3-KCl, 25.0 ml. {NaOH, 22.0 ml.	.128	.063	.044	.036	.031	.025	.023	.021	.018	.022
10.8	{Na_2HPO_4, 25.0 ml. {NaOH, 4.13 ml.	.209	.101	.074	.065	.057	.053	.050	.045	.038	.032
11.8	{Na_2HPO_4, 25.0 ml. {NaOH, 21.6 ml.	.545	.163	.104	.089	.080	.070	.061	.052	.045	.038

[a]These solutions are M/5 with respect to each constituent.

Stuckey recommended that conditions of analysis prevail which will ensure complete ionization and for solutions of weak bases a strongly acid pH is necessary to "stabilize" the spectrum so that it is unaffected by small pH changes. Stuckey states that the spectra of morphine, codeine and diamorphine (diacetylmorphine) as salts are very similar, the absorption in acidic solutions being low ($E\,\frac{1\%}{1\text{ cm.}}$; 280 mμ ca. 50); morphine in alkaline solution shows a much higher absorption $E\,\frac{1\%}{1\text{ cm.}}$; 258 mμ ca. 310, presumably due to the phenolic group. Apomorphine absorbs more strongly in acid solution ($E\,\frac{1\%}{1\text{ cm.}}$ 373 mμ ca. 600) and this property can be used for its analysis in tablets and pharmaceuticals (53).

Seagers, Neuss and Mader (1952) measured the ultraviolet spectrum of N-allylnormorphine in water solution and found a maximum at 285 mμ and a minimum at 260 mμ (54). Addition of acid caused no change in the spectrum, but alkali caused a considerable increase in absorbance and a bathochromic shift of maximum to 298 and minimum shift to about 278 mμ. The ultraviolet chromophore present in N-allylnormorphine, morphine, normorphine, and related compounds, is the hexadrophenanthrene ring, according to Seagers *et al.*, to which chromophore the authors attribute the similarity of the ultraviolet spectra of all opiates (54).

Biggs (1952) has applied spectrophotometry to the detection and estimation of morphine in Stas-Otto extracts from viscera and natural products (55).

Biggs (1953) examined the spectra of cannabis extracts and found their absorption curves are characterized by a band with pronounced ultraviolet absorption. Figure 14 shows extracts of *Cannabis sativa*, both saponified, and unsaponified, and cannabis extract from the viscera; figure 15 shows extracts of *Cannabis sativa* mixed with tobacco. The absorption bands are attributed to cannabinol and cannabidiol (55).

Smith and MacDougall (1953) published a compilation of ultraviolet absorption data of compounds of toxicological interest (56). This work has been critically evaluated by Morgan (57). Brackett and Bradford (1953) have published a compilation of about 85 spectra of which 15 are narcotics (58).

Clark and McBay (1954) have utilized the spectrophotometric spectra of morphine in different media at different pH's to determine these substances (59). As means for identification of morphine and codeine the authors state: "This method of identification is valid only if the substance to be identified is suspected to be either morphine or codeine. Many substances, particularly other alkaloids of opium, may possess the same maxima as do morphine and codeine in alkaline media" (Baggesgaard-Rasmussen (60)).

Umberger (1954) in an excellent chapter on "Analytic Toxicology" describes the application and recent advances in the use of ultraviolet spectrophotometry for identification of drugs (61). Kaye and Goldbaum (1954) in a recent text (62) describe the application of spectrophotometry to the analysis of 33 drugs at two different pH values.

7. Quantitative spectrophotometry

For the greater part the review of literature has been up until now concerned with qualitative identification

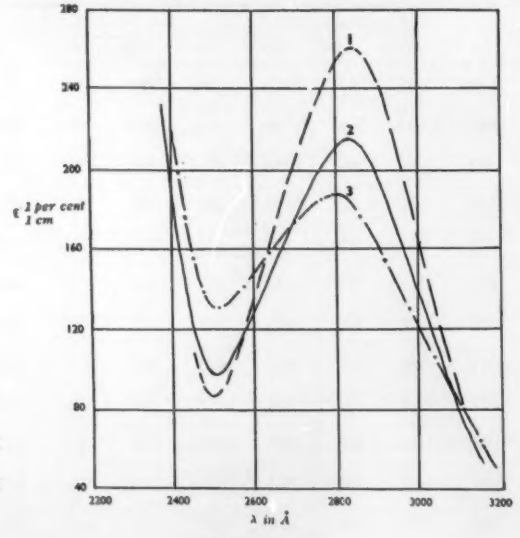


FIGURE 14

Spectra of Cannabis sativa *extract, according to Biggs (1953)*

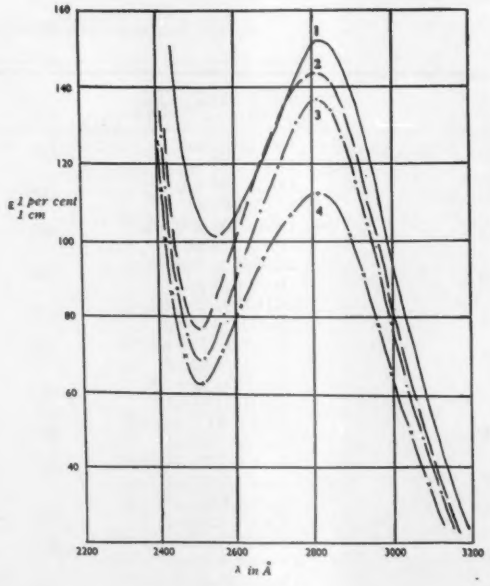


FIGURE 15

Spectra of Cannabis sativa *mixed with tobacco, according to Biggs (1953)*

of narcotics by spectrophotometry. Quantitative determinations require a more precise knowledge of the influence of different variables upon the absorption energy. The simplest case of absorption is that of a parallel beam of monochromatic radiation passing rectilinearly through a homogeneous absorbing medium. The intensity of this beam is reduced by the same fractional part by each succeeding portion of its path under these conditions. Thus if the intensity is reduced by one-third in the first millimeter, it will be reduced to one-ninth of its original intensity by the second millimeter. This fact was first enunciated by Bouguer in 1729. It was later applied by Lambert, and sometimes is called Lambert's Law. According to Timma (63) when dealing with solutions in which molecules are acting as energy absorbers, the optical path may be varied either by changing the cell thickness (see Hartley's early work, 1884-1907) or by changing the concentration of the solute. The latter method is often called Beer's Law. However, in a critical examination of Beer's paper (1852) (64) Pfeiffer and Liebhafsky (1951) point out that (1) Beer's paper does not contain an absorption law in which concentration appears as an explicit variable; (2) Beer thought primarily of amount or mass of absorbing material; (3) Beer may or may not have understood the functional relationship between absorbence and mass (or concentration) of absorbing material, at any rate he used length as an intermediate variable in correlating results obtained at different dilutions.

There is no evidence in Beer's paper to indicate that he believed he had discovered a new absorption law. The phrase "Beer's Law" occurs forty years later (1889) in the writings of Walter. It was in Kayser's *Handbuch* (1905) that we find the statement of the attributing of the law to Beer as follows: "If we let *a* represent the absorption coefficient for unit concentration, there follows the absorption law

$$I = I_0 a^{cd}$$

where d is the thickness of the layer and c the concentration. The law was set up by Beer and is called "Beer's Law". According to Pfeiffer and Leibhafsky: "There is thus good precedent for any twentieth century inaccuracies in describing what Beer thought and did."

Regardless of the origin the familiar expression of the Beer's Law is $E = Kcd$. where K=specific absorption coefficient, c is the concentration, and d is the sample thickness. Quantitative determinations consist of measuring the absorbency of a sample at wave-length or a narrow range of wave-lengths and correlating the extinction with concentration. Quantitative determinations involve the solving of simple algebraic equations (Friedel and Orchin) if the absorbencies are additive. If not additive quantitative determinations become empirical and depend upon the previous determination of a working curve showing the absorbency-concentration relationship.

While many instances are known where Beer's Law is said to be valid, deviations are both frequent and significant. Kortum (1936) has stated "that the validity

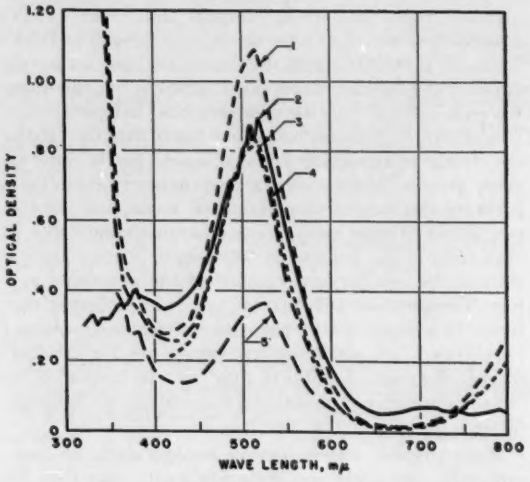


FIGURE 16

Absorption spectra of red colored solution produced from porphyroxine-meconidine by different spectrophotometers. Curve 1. *Slit width 1 mμ at 512 mμ.* Curve 2. *Slit width 32 mμ at 512 mμ.* Curve 3. *Slit width 1 mμ at 512 mμ and cell 1.3 cm.* Curve 5. *Lower concentration of colored material*

of Beer's Law for ions must be considered as an exception rather than as a rule". Validity over large concentration ranges is not to be expected since Beer's Law is a limit law for low concentrations (65).

The deviations from Beer's Law are of two types—instrumental and chemical or physical. It is generally held that a linear Beer's Law plot of absorbence $\log \frac{I_0}{I}$ versus concentration of an absorber is indicative of a linear response of the detecting system of the spectrophotometer. The results reported by Cannon and Butterworth (1953) demonstrate theoretically and practically that this is a fallacious assumption (66). A nonlinear spectrophotometer, although giving a linear Beer's Law plot, will give erroneous values for absorptivity; absorbences are too low, i.e., the slope of the analytical calibration curve will be changed. Absolute tests of linearity of response of spectrophotometers should be made to determine the magnitude of the non-linearity error in absorbence value. Other instrumental sources of error appear to have been restricted to the effects of stray light and finite slit width. What may be attributed to a deviation from Beer's Law may be a low degree of monochromaticity of the radiant energy used. Even the best monochromators give a spectral band of finite width, and apparent deviations will be noted if the absorbency of the sample changes considerably across the spectral interval isolated by the monochromator (67) (Brattain, Rasmussen, and Cravath (1943), see figure 16). Poor matching of absorption cells and stray radiation may also be factors.

Physico-chemical changes in the absorbing material more often cause the deviations from the law than do

failures in the law itself. Kortum and Seiler (1939) summarized the causes for divergence from the Beer's Law (65). According to the theory of light dispersion it is not the specific absorption coefficient but the quantity $Kn/(n^2+2)^2$ which is a constant, independent of concentration. For concentrations lower than 0.01 molar the change in refractive index, n, would rarely cause an error greater than the accuracy of measurements. Temperature fluctuation may influence absorption data in two ways. It may cause concentration changes due to expansion of the volume of solution, or it may cause a shift in the equilibrium constant of the absorbing system. Temperature effects may vary with different material. It amounts to 0.1 per cent per degree at 436 mμ for chromate ion and 1 per cent per degree for 2,4-dinitrophenolate ion. Equilibria may also be displaced by the presence of non-absorbing materials in the solution through the mass action law.

Many organic materials have weakly acidic or basic properties and their equilibria are easily disturbed by changes in acidity. For this reason it is often necessary to control the pH of the solution within narrow limits to obtain reproducible results.

8. The influence of pH on ultraviolet spectra of drugs and its use in their determination

The change in absorbence, location of wave-length of absorption maxima, and number of maxima of absorption spectra of many substances at different pH's has long been known. Increasing use of this property has been made both in qualitative and quantitative spectrophotometry.

About 1830 Stokes (24) noted the increased fluorescence of quinine dissolved in sulfuric acid (see figure 17). Fischer (33) (1925) related the enhanced ultraviolet absorbence of quinine in N/10 HCl and/or N/10 H_2SO_4 to that of quinine sulphate in water alone. He showed the difference in the position and intensity of the absorption bands in acid and basic media. This work was done in the Forensic Medicine Institute of the University of Zurich.

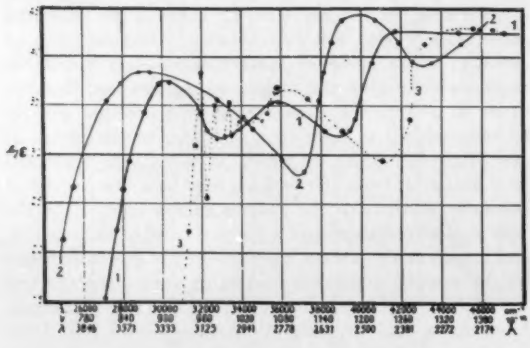


FIGURE 17

Effect of pH on quinine sulfate, according to H. Fischer (1925)

In 1921 Pringsheim (68) showed that aniline and naphthylamine solutions have absorption spectra which in hydrochloric acid become very similar to benzene and naphthaline absorption curves, similarly the quinine curve in hydrochloric acid becomes more like the quinoline curve. Brode (1924) showed that the change of pH value of solutions of indicators results in a change in intensity rather than a wave-length shift of the absorption band; thus one resonating system is eliminated and another is formed (69). This change from one system to another is inversely proportional to the relative extinction coefficients, and hence there will be a point of extinction on the curves where the pH has the same value. Such a point is known as the isobestic point.

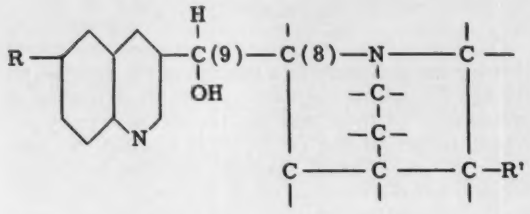
The effect of pH on the band maxima location of amines has been noted by many other workers. Kato and Someno (1937), Wohl (1939), Sklar (1939) showed that aniline has about 1/50 the absorption in acid that it has in water. Dede and Rosenberg (1934) explained this effect of resonance theory whereby the "lone" electrons on the nitrogen atom were unable to migrate from the amino group to the benzene ring in acid and thus the anilinium ion spectrum reverts to the benzene spectrum. Kumler and Strait (70) extended this theory to fit any aromatic amino compound converted to a salt.

Kumler and Strait obtained a spectrum of sulfanilamide in sodium hydroxide with increased absorbances compared to the spectra in neutral and acid solutions. Bell, Bone and Rollin (71) (1944) were unable to confirm this result and showed differences in spectra obtained by Kumler and Strait (70) were due to absorption by sodium hydroxide solution. The importance of using ultraviolet transparent buffers in pH studies or else compensating blanks containing similar concentrations of ions should be noted. A set of ultraviolet transparent buffers for pH studies in this region was devised by Morgan (*loc. cit.*) and is reproduced in table IV.

Vandenbelt and Doub (1944) made an extensive study of the absorption spectra of sulfanilamide derivatives and characterized them with respect to change in pH (72). They were able to associate the spectral bands with absorbing groups in the molecule as follows: 257-259 mμ due to sulfanilamide portion, 280-283 mμ due to thiazole portion (258 mμ=thiazole structure); peak at 311 due to pyridine in sulfapyridine, band at 261 due to sulfanilyl portion, 241 mμ due to pyrimidine ring.

Stimson and Reuter (1946) (73) studied the problem of estimating the methoxyl cinchona alkaloids in crude extracts. The four common natural occurring alkaloids and some related compounds were also measured over a pH range of 1-10. The maximum at 280 mμ in quinine, quinidine, epiquinine, and epiquinidine disappears and becomes a minimum at pH 4, 3, 1, and 1 respectively. There is a well defined invariant point (isobestic point)

in the levo bases quinine and cinchonidine located at 295 mμ in both cases, which may be related to the optical configurations of these compounds and may show that the energy distributions accountable for the appearance of these isobestic points are destroyed by epimerism at either C_8 or C_9 of the molecule, as shown:



Morgan and Caprini (1947) made a further study of the effect of pH on sulfanilamide spectra to clear up the discrepancies in previous findings, and as a preliminary study for extensive work on the pH effect on spectra of many other drugs. A summary of the findings of various workers is included in table V (34).

Table V

EFFECT OF pH ON ABSORPTION MAXIMA OF SULFANILAMIDE

Acid or pH value	*λ max*	*E*	*Reference*
2 N HCl ...	260	600	Vandenbelt and Doub
0.8 N HCl ..	260	620	Kumler and Strait
pH 1.1	259	4,320	Morgan
pH 7.0	258-259	16,160	Morgan
M/1 NaCl ..	258.5	16,380	Bell, Bone, Rollin
M/1 NaCl ..	258.0	14,130	Kumler and Strait
pH 7.0	260	16,500	Vandenbelt and Doub
pH 11.8	251.0	16,170	Morgan
M/1 NaOH.	250.5	16,150	Bell, Bone, Rollin
1N NaOH ..	257.0	15,850	Vandenbelt and Doub

In 1940 Elvidge had determined the pH dependence of morphine, diacetylmorphine, codeine and apomorphine (39). The spectral data in acid, base, and neutral (H_2O) solutions as determined by Elvidge are given in table VI.

Kumler *et al.* (1948) studied the effect of pH on the spectra of amidone etc. (see above). Foster and MacDonald (1951) studied papaverine spectra at a number of pH values. The results of their work are listed in table VII (51).

Table VI

ABSORPTION MAXIMA, MINIMA, AND EXTINCTION VALUES ($E^{1\%}_{1\ cm.}$) FOR SOME NARCOTICS, ACCORDING TO ELVIDGE (1940)

Substance	*Solvent*	*Maxima at* mμ	*Maxima at* $E^{1\ per\ cent}_{1\ cm.}$	*Minima at* mμ	*Minima at* $E^{1\ per\ cent}_{1\ cm.}$
Morphine alkaloid	Isopropyl alcohol and N/2 HCl	282	56	263	19
Morphine alkaloid	N/1 sodium hydroxide	276	95	278	55
		258	310	245-255	260
Diamorphine alkaloid	Isopropyl alcohol and N/2 hydrochloric acid	282	56	256	19
Codeine alkaloid	Isopropyl alcohol	279	42	265	20
Codeine phosphate	Water	280	44	265	30
Apomorphine hydrochloride	Water and N/2 hydrochloric acid	273	670	248	220
		305	200	299	130
		315	165	310	145
		324	120	321	115

In regard to the effect of pH on the spectra of phenols, naphthols and enols, Morton (1925), Tipping (1927) and Stenstrom (1925, 1926) showed that a shift to longer wave-lengths occurs when these hydroxyl compounds pass from neutral to basic solution since the ion absorbs at lower wave-lengths than the unionized compound (74).

The effect of pH on the spectra of acids (salicyclic) and esters (acetylsalicyclic) was thoroughly studied by Edwards (1950). Below pH 1 each of these acids was regarded as undissociated, while above 6 the dissociation was substantially complete. The key points of the absorption curves are given in the table VIII (75).

Table VII

EFFECT OF pH ON THE ABSORPTION MAXIMA AND MINIMA OF PAPAVERINE HCl WITH EXTINCTION VALUES ($E^{1\%}_{1\ cm.}$), (from Foster and MacDonald (51))

pH	*Maxima* mμ	*Maxima* $E^{1\%}_{1\ cm.}$	*Minima at* mμ	*Minima at* $E^{1\%}_{1\ cm.}$
1.5	250	1800	270	180
	309	240	—	—
3.95	251	1595	—	—
	—	—	—	—
6.3	245	1285	—	—
	—	—	—	—
9.0	238	1700	—	—
	—	—	—	—
11.0	238	1900	262	260
	276	290	—	—

Table VIII

KEY POINTS IN THE ABSORPTION SPECTRA OF SALICYCLIC ACID AND ASPIRIN (after Edwards 1950)

Compound	*Form*	λ (mμ)	*E*	
Salicylic acid	Molecular	236	8350	Maxima
		302	3620	
		261.5	300	Minimum
	Ionic	228.5	6920	Maxima
		296.5	3520	
		263.5	590	Minimum
		229.5	6890	
		249.0	1900	Isobestic
		298.5	3470	points
		327	510	
Aspirin	Molecular	275	1160	Maximum
		259	760	Minimum
	Ionic	None		
		No isobestic points		

The carbinol-ammonium equilibrium is affected by pH and the spectra of cotarnine at different pH's reflect these shifts. This was first noted by Dobbie (1903). Hartley (1885), Dobbie (1903), Brustier (1926) and Kitasato (1927) were the first to measure the spectrum of narcotine and to illustrate the effect of pH on its spectrum data. These shifts are due to the change from a lactone form in acid to an alkali salt in base.

As a result of the increased interest in recent years, since about 1950, of scientists in the spectra of compounds at different pH's, several collections of spectral data for drugs at different pH's have been made. Morgan (*loc. cit.*) has made an extensive collection most of which is unpublished. Smith and MacDougal (1950) have published (56) a collection of data at two pH's for 154 different compounds. Goldbaum (1954) has recently published a list of about 85 compounds and spectral data in 0.5 N NaOH and 0.5 NHCl. Levi and Beaudry (1953) have collected the spectra of twenty-four barbiturates at 5 different pH's 3, 5, 9, 11 and 13. Brackett and Bradford (1952) have published 132 spectra. Beckman Instruments, Inc. (Nov. 1954) has offered to inaugurate a collection of ultraviolet curves of 50 common compounds at 3 pH levels. H. J. Noebels (76) is in charge of this project. There is no doubt that these collections of spectra will be of potential value to analysts in the identification of drugs; however, cross-checking and comparison of the data in these above collections with one another and with data already in the literature from other sources indicates an alarming conflict. The maxima and minima appear to be in reasonable agreements but the extinction coefficients are very different, a factor of 8 times being noted in some cases. Morgan (1954) has already pointed out the necessity for critical review of the data before it is put at the disposal of forensic scientists. Compounds having spectra greatly influenced by pH should be thoroughly checked, others easily oxidized in alkaline solution have spectra which change rapidly with time. Impurities in some of the "standards" used should be checked, authenticity should be established as thoroughly as possible. Nomenclature of the compounds can be quite confusing and generic or chemical names should be used as often as possible in compilations. It should be possible for the scientists concerned to decide on a uniform method of presentation of data and a critical examination of the present material in the literature. Apparently forensic scientists are not alone in this state of confusion.

9. TREATMENT OF DATA

Qualitative data are generally presented as curves showing the absorbence as a function of the wave-length through the spectral range covered. No single method of presentation of these data has become universally accepted. In fact, Mellon (77) (1949) has said "the confusion in usage, terms, symbols, and data in absorptiometry remains unsurpassed by that in any other division of quantitative analysis". One might add that there has been very little improvement in the past five years.

The ordinate is usually plotted in increasing values of transmittance, T, absorbency, A (also known as optical density or extinction) ε or E, extinction coefficient, k, or absorbency index, as, molecular extintion, ϵ (or molar absorbency index, Am) and lately absorbence, or the logarithm of any of them. The abscissa is used to present the region of the spectrum investigated and may be expressed in one or more of the following terms: wave-length, λ, (in millimicrons mμ, or Ångstroms, Å); frequency, ν (in fresnels); wave-number, $\bar{\nu}$ or ν (in waves per centimetre); or the logarithm of the wave-length. Wave-length, wave-number and frequency are related by the expression

$$\frac{1}{\text{Wave-length}} = \text{Wave-number} = \frac{\text{Frequency}}{\text{Speed of light}}$$

With all the possible combinations in use including inconsistency in the direction of plotting, and disregard for general good graphing practice the literature is less than clear. Friedel and Orchin (21) have gone so far as to present a scheme for transforming the various relationships with which one ordinarily deals (2). Instrument measurements such as optical density (absorbence) and transmittance are often plotted directly from the instruments because of convenience, sometimes without any supplementary information regarding solvent, concentration, pH, etc.

Quantitative absorption spectrophotometry depends upon the correlation of the amount of energy absorbed at a given frequency with the amount of material present in the sample. This correlation is known as a working curve or calibration curve and consists of plotting the absorbence, or transmittance, as a function of concentration. Ringhom (1939) suggested plotting working curves of absorbency vs. the logarithm of concentration to emphasize the importance of making measurements within certain absorbence ranges where the error of measurement is smallest. If the transmittancy can be read to ±0.5 per cent, the maximum accuracy will be 1.4 per cent according to Peterson (1949). This is attained when the absorbency equals 0.4343 (36.8 per cent transmittancy). Ayres (34) stated that the mini-

mum error in absorbency occurs at 0.5550 (28 per cent transmittancy). Sobel (34) has given the following table IX relating the concentration to absorbency, which was obtained from Morgan and Peterson's paper (34).

10. Conclusions

Morgan (34) advocates the use of the "baseline" procedure for calculating percentage in unknown solutions where the background absorption is considerable.

Absorption spectrophotometry offers a rapid accurate method for qualitative and quantitative analysis of narcotics. The historical development of the theory and application of these methods in relation to narcotics has been reviewed. The first work was done in 1885, and the first application in forensic cases was advocated at this time. About 1922, the use of spectrophotometry in the medico-legal field developed to a considerable extent in Europe. The latest development in this field has been the use of the pH shift for characterizing spectra and thereby closely related compounds can be more easily discriminated.

Table IX

Relation of concentration to absorbency (34)

Absorbency	*Transmittancy*	*Error in concentration, per cent*	
		Scale ± 0.5%	*Scale ± 0.1%*
1.000	10	±2.17	±0.43
0.699	20	±1.55	±0.31
0.523	30	±1.37	±0.27
0.4343	36.8	±1.36	±0.27
0.398	40	±1.38	±0.28
0.301	50	±1.44	±0.29
0.222	60	±1.63	±0.33
0.155	70	±1.94	±0.39
0.097	80	±2.80	±0.56
0.046	90	±4.90	±0.90

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Part III B. Ultraviolet Spectral Data for Ninety Narcotics and Related Compounds

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Introduction

The purpose of this paper is to present the experimental results of a survey of narcotics by means of ultraviolet spectrophotometry, consisting of summaries of ultraviolet absorption data, tables of maxima, minima and molecular extinction coefficients and spectra for ninety narcotics and related compounds for use in identification.

Résumé of methods of presentation of spectral data

There are various ways of recording ultraviolet spectral data. They are often presented in tabular form showing simply the value of the absorption maxima, or as a table of maxima and minima. Some tables include intensity values expressed either as $E\,^{1\%}_{1\,cm}$ or as ϵ or as absorbence referred to a concentration, at the corresponding maximum and minimum wave-lengths. A table listing maxima and minima and intensity values is most valuable because it permits the construction of a rough graph of the actual spectral curve.

There are a few conventions to be noted in the presentation of spectral data in graphic form. Spectral data are always plotted so that, in the final graph, the abscissae represent either the wave-lengths expressed as millimicrons or angstroms, or the frequencies expressed as sec.$^{-1}$ or fresnels, or the wave numbers expressed as cm.$^{-1}$ or mm.$^{-1}$. Wave-length values are usually plotted increasing to the right. The ordinates represent values for the intensity of absorption which may be expressed in several ways, either as absorbence, transmittance, specific extinction coefficients, K, or $E\,^{1\%}_{1\,cm}$, molecular extinction coefficient, ϵ, or as a log function of any of these values.

A variety of curves may be obtained for the ultraviolet spectra of a compound depending on the different units used for plotting abscissae and ordinates.

The abscissa of the spectral graph

The abscissa of a spectral graph may be expressed in terms of wave-length, frequency and wave number. These are discussed under sections (*a*), (*b*), (*c*) below and illustrated in plates I and II.

(a) *Wave-length*

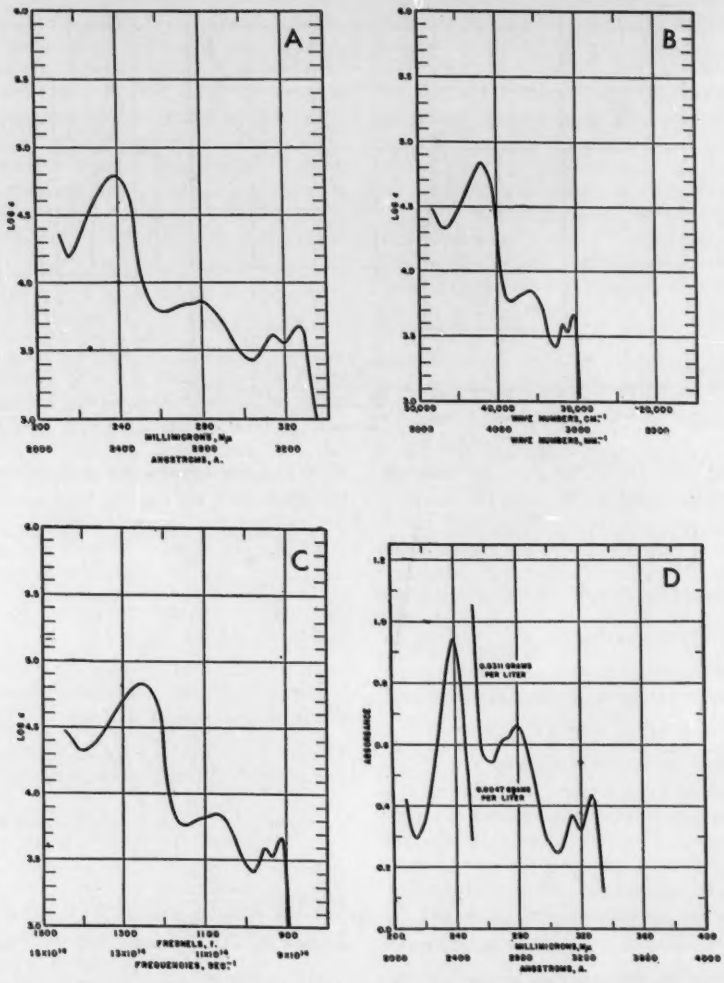
Most ultraviolet spectrophotometers are now calibrated to give wave-length readings directly. It is convenient to express the abscissa as such in graphing these readings. The wave-length readings commonly used in graphs of spectra are as follows:

1 Å (angstrom)$=10^{-8}$ cm.$=10^{-10}$ m.
1 mμ (millimicron) $=10$ Å $=10^{-7}$ cm.
1 μ (micron)$=10{,}000$ Å$=1{,}000$ mμ.

These wave-length units were used in plates I and II, parts (A), (D), (E), (F), and (G), as illustrations of the different possible plots.

(b) *Frequency of oscillation of the wave* ($\bar{\nu}$, *sec*$^{-1}$)

Frequency is an expression of the number of waves per unit of time, usually per second. Corresponding to each point of the spectrum there is a characteristic frequency or number of vibrations per second. This is a more fundamental unit than wave-length and is used for theoretical studies. For ordinary purposes the relationship between frequency and wave-length may be expressed by the formula $\bar{\nu} = c/\lambda$, where λ is the wave-length in cm., c is the speed of light in cm. in the medium. Another unit, the fresnel, is also used to express the frequency of oscillation of the wave. Its relationship to $\bar{\nu}$, sec.$^{-1}$ is shown in the following formulae:



1 fresnel (f) = 10^{12} vibrations per second
1 fresnel=frequency, sec.$^{-1}$ x 10^{-12}

f, since it is smaller than $\bar{\nu}$ sec.$^{-1}$ is sometimes used for convenience. The frequency plot is illustrated in plate I (C).

(c) *Wave number ($\bar{\nu}$ cm^{-1} and $\tilde{\nu}$ mm^{-1})*

The wave number expresses the number of waves per unit length, either one centimetre or one millimetre, of the light path *in vacuo*. Wave number is related to wave-length according to the following equation:

$\lambda\bar{\nu} = 10^{-8}$, where λ = Å, $\bar{\nu}$ = cm^{-1}.
$\bar{\nu}$ cm^{-1} = $1/\lambda$ in cm.

Wave numbers, like frequencies, are more fundamental than wave-lengths. The wave number plot is illustrated in plate I (B).

THE ORDINATE OF THE SPECTRAL GRAPH

Intensities, as ordinate values expressed as different units, may be plotted in two ways, **A** and **B.**

A. *The absorption curve in which the high intensity values define the band maxima*

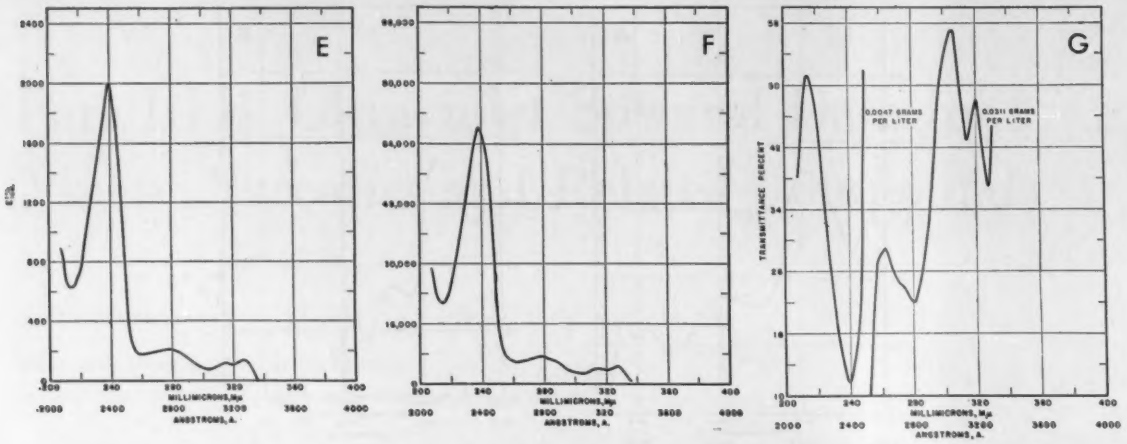
(a) *Absorbence (A), formerly called optical density or — log T, referred to a specific concentration*

The absorbence data obtained from a Beckman instrument may be plotted directly on a graph. One disadvantage of such an absorbence plot is that in plate I (D). A single curve does not usually result, since a separate curve is obtained with each appreciable change in concentration.

(b) *Specific extinction coefficient, (K) expressed in g. per l.*

The formula used for calculating K is as follows:

$K = \frac{A}{c}$, where A=absorbence and c=concentration, g./l. The K plot results in a single curve over the entire concentration range.



(c) *Extinction coefficient for a one per cent solution referred to a one centimetre cell*

$$\left(E\,\frac{1\%}{1\text{ cm.}}\right)$$

$E\,\frac{1\%}{1\text{ cm.}} = 10K$. The spectra of unknown materials from natural sources are usually plotted as $E\,\frac{1\%}{1\text{ cm.}}$ since no knowledge of molecular weight is necessary and a single curve results. The type of curve obtained is illustrated in plate II (E).

(d) *Molecular extinction coefficient* (ϵ)

In addition to yielding a single curve, the plotting of ϵ values may allow some grouping of the spectra of structurally related compounds. The molecular weight appears as a factor in the calculation, making it possible to compare the spectra of compounds of different molecular weights. The molecular extinction coefficient plot is illustrated in plate II (F).

(e) *The logarithm (to the base 10) of any of the intensity values, K, ϵ, $E\,\frac{1\%}{1\text{ cm.}}$*

Log ϵ is the most commonly employed intensity function. It serves the same purpose as the ϵ plot and has several additional advantages. The log ϵ plot expands the weaker absorption bands which are often obscured in the ϵ plot. When plotting spectra where the ϵ max. values are very high and the ϵ min. values are very low, a change in scale is often required. When studying the spectra of a large number of compounds these changes are undesirable. The log ϵ plot overcomes this difficulty. Illustrations of the log ϵ plot are shown in plate I (A), plate I (B) and plate I (C).

B. *The absorption curve in which the low intensity values define the band maxima*

(a) *Transmittance or per cent transmission*

Transmittance is inversely proportional to absorbence, as can be seen by comparing plate I (D) with plate II (G). The advantages and disadvantages of the absorbence plot also apply to the transmittance plot.

(b) *Equivalent thickness of the absorption solution layer in mm. or cm.*

This method of plotting intensity is now obsolete, but was used in the early literature. See figure 2, curve 1, and figure 9, part III A (1).

Interconversion of various ordinate values

The following scheme of conversion was given by Friedel & Orchin (2) for comparing literature spectra plotted with different intensity units.

Operation	*Literature Value*	*Unknown Spectra*	*Operation*
	Log ϵ	Log ϵ	take log
take antilog →	ϵ	ϵ	multiply by M
divide by M →	K	K	divide by b.c.
multiply by b.c. →	A	A	(measured)

where M = molecular weight of the compound
c = concentration of solution in g./l.
b = thickness of absorption cell in centimetres.

Preparation of materials

The preparation of materials used in this paper has been dealt with in part I B (3).

Apparatus

The Beckman DU model ultraviolet spectrophotometer was used with one centimetre silica absorption cells.

Solvents

The solvent used in the preparation of solutions for the ultraviolet absorption spectra of the free narcotic bases was in most cases reagent grade absolute ethanol. Since cryptopine base and pseudomorphine base were

both insoluble in absolute ethanol, in these cases 0.02 N HCl was used as solvent. Distilled water was used to prepare solutions of the narcotic salts. A solution of mescaline sulphate was also prepared using 80 per cent ethanol as solvent. Two solutions of cotarnine base were prepared using absolute ethanol and water. These solutions were later acidified with a few drops of concentrated HCl. Distilled water was used to prepare a solution of morphine-N-oxide. All the solvents used were found to be spectrally pure and no further purification was necessary.

Procedure

As a routine, for compounds whose spectral characteristics were unknown, the following procedure was used. Approximately 12.5 mg. of the compound were accurately weighed, placed in a 25 ml. volumetric flask and "made to volume" with the appropriate solvent. This stock solution (0.5 g. per l.) was accurately diluted to yield a 1:5 solution (0.1 g. per l.). The spectrum of the 1:5 solution was then rapidly obtained in the region 205-340 mμ. at intervals of 10-20 mμ. to determine if the 1:5 concentration was suitable, i.e., if the corresponding absorbence values at the maxima lie in the range 0.250-0.600. If the 1:5 dilution allowed the maximum absorbence to fall within these limits, the curve was more exactly determined from 205 mμ. using another portion of the 1:5 solution. Absorbence readings were taken every 2 mμ. for the major portion of the curve and every 1-0.5 mμ. in the regions of maximum and minimum absorption. When the preliminary determination of the spectrum showed the absorbance values of the maxima to be above 0.600, a portion of the 1:5 solution was further accurately diluted and a more exact determination was made. If the preliminary determination of the spectrum showed the absorbence values at the maxima to be below 0.250, a new solution was prepared from the stock solution and a more exact determination of the spectrum was made. In most cases, another dilution was necessary for measuring absorbences in the region 200-240 mμ. One concentration of solution however could be used to obtain the entire spectrum in the cases of meconic acid, opianic acid, thebenine HCl and cotarnine.

For the purpose of plotting the spectral curves, absorbence values were converted to molecular extinction coefficients, ϵ, according to the formula:

$$(1)\ \epsilon = \frac{\text{absorbence} \times \text{molecular weight}}{\text{concentration (grams per liter)}}$$

The molecular weights of narcotics shown in table I, part I B (4), used to calculate ϵ, include the total molecular weight of water added to the anhydrous molecular weight of the narcotic. The measured absorbence and concentration values were used in formula 1. An extinction value for each absorbence reading was thus obtained.

The ϵ values were then plotted as ordinates on semilog paper against the wave-length in millimicrons as abscissae. This graph was then traced onto an ozalid grid. The ozalid grid showed log ϵ as ordinates and wave-length in millicrons as abscissae. ϵ values of 10, 100, 1000, etc., correspond in position on the ozalid grid to log ϵ values of 1, 2, 3, etc. This method of graphing on previously prepared grids eliminated the need to convert each ϵ value to its log ϵ equivalent before plotting. The structural formula and the chemical or common name of the narcotic base was then mounted on the grid along with the chemical formula of the substance studied. The solvent employed was also shown. The legend on the spectra in most cases, ". . . . . Base (B) ethanol", indicates that the spectra are that of the base, symbolized by the letter "B". The legend, ". . . . . BHCl water", indicates the spectra of the salt dissolved in water. In cases where a single graph was given a heavy line may indicate the compound BHCl or other salt, e.g., $B_2H_2SO_4$, etc.

Results

Table I shows U.V. maxima in increasing order of wave-lengths. This table is intended to serve as a reference for the ultraviolet absorption analyses of unknown narcotics and related compounds and to illustrate the spectral relationships present in the compounds studied. All the wave-lengths of maximum absorption of each compound are included.

Table II shows spectral data arranged according to chemical families. The compounds in this table are arranged according to the main chemical classification shown in part I A (5). The table includes wave-lengths of maximum and minimum absorption and corresponding ϵ values and concentrations in g./l. The number following the name of the compound refers to the number of the spectrum.

The spectra of the ninety compounds studied are given in fifty-six graphs. The spectra are arranged and numbered according to the chemical classification given in part I A (6).

General discussion of results[1]

Certain correlations between structure and ultraviolet spectra are discussed in the following paragraphs. A number of the main chemical groupings including examples from each family are discussed first, followed with comments on the important spectral characteristics related to the structure.

Pyran spectra

Two compounds, meconic acid and pyrahexyl, are included in the pyran group. Meconic acid contains two carboxyl groups and a ketocarboxyl group and is a single ring substituted pyran. Pyrahexyl contains a phenolic OH group and is a dibenzopyran.

The spectra of meconic acid (figure 1) and pyrahexyl (figure 2) are distinctly different. The meconic acid

[1] The figure numbers in the "General discussion of results" refer to spectra figures 1 to 56 inclusive.

Table I

SPECTRAL DATA SHOWING ABSORPTION MAXIMA IN INCREASING ORDER OF WAVE-LENGTHS

Maxima wave-length λ *mμ.*	*Compound*
208	narceine HCl
208-209	ethylnarceine HCl
209	morphine HCl narcotine base opianic acid morphine-N-oxide
209-210	N-allylnormorphine HCl
210-211	meconic acid
211	morphine H_2SO_4 apomorphine HCl narcotine HCl ethylmorphine HCl
211-212	codeine base
212	codeine H_3PO_4
213	benzylmorphine HCl
217	morphothebaine HCl
217-218	thebenine HCl
218	dextromethorphan HBr
218-219	ecgonine
219	racemethorphan HBr racemorphan base (Dromoran® base)
219-220	levomethorphan HBr
220-221	racemethorphan base
229	pseudomorphine base pyrahexyl base
230	opianic acid cocaine base
233	cocaine HCl
234	cryptopine base meconic acid
239	papaverine base
244-245	phenacetin
249	hydrastinine Cl
249-250	papaverine HCl
251	alphaprodine HCl ethylpethidine HCl
251-252	pethidine HCl
252	pethidine base alphaprodine base betaprodine HCl dioxyline H_3PO_4
253	*dl*-methadone HCl *d*-methadone HCl *l*-methadone HCl *dl*-α-methadyl acetate HCl *d*α-methadyl acetate HCl *d*-α-methadyl acetate HCl phenadoxone HCl
254-255	cotarnine base—water
255	cotarnine base—water + HCl
255-256	cotarnine base—ethanol
257	thebenine HCl alphaprodine HCl betaprodine HCl pethidine HCl ethylpethidine HCl
258	alphaprodine base pethidine base pipidone HCl *d*-α-methadyl acetate HCl *d*-α-methadyl acetate HCl *l*-α-methadyl acetate HCl
258-259	cotarnine base—ethanol + HCl isomethadone HCl isomethadone base
259	*dl*-methadone base *dl*-methadone HCl *d*-methadone base *d*-methadone HCl *l*-methadone base *l*-methadone HCl pipidone base phenadoxone HCl
259-260	phenadoxone base
263	alphaprodine HCl betaprodine HCl pethidine HCl ethylpethidine HCl
264	pethidine base pipidone HCl alphaprodine base isomethadone HCl *dl*-methadone HCl *l*-methadone HCl
265	*d*-methadone HCl isomethadone base pipidone base phenadoxone HCl sinomenine HCl
268	morphothebaine HCl
269	mescaline H_2SO_4—water mescaline H_2SO_4—80% ethanol trichocereine HCl
270	narceine base acetoxyketobemidone HCl
272	acetoxyketobemidone HCl apomorphine HCl
273	caffeine base
273-274	acetylsalicylic acid
274	cocaine base cocaine HCl
274-275	ecgonine base
275	Bemidone HCl
276	morphothebaine HCl
276-277	pyrahexyl base
277	Bemidone base narceine HCl ethylnarceine HCl
278	racemethorphan HBr dextromethorphan HBr levomethorphan HBr diacetylmorphine HCl
279	levorphan tartrate (*l*-Dromoran® tartrate)
279-280	papaverine base racemorphan HBr (Dromoran® HBr)
280	Acedicon® HCl Dicodid® bitartrate Dilaudid® HCl Eukodal® HCl ketobemidone HCl methylketobemidone HCl
281	racemethorphan base diacetylmorphine base papaverine HCl cocaine base ketobemidone base propylketobemidone base
281-282	methylketobemidone base
282	metopon HCl
282-283	Dicodid® base Dilaudid® base
283	Eukodal® base laudanine base opianic acid racemorphan base (*dl*-Dromoran® base)
283-284	ethylmorphine HCl benzylmorphine HCl
284	neopine HBr codeine H_3PO_4
284-285	dihydrocodeine base metopon base Paveril® H_3PO_4
285	morphine H_2SO_4 morphine HCl morphine HI morphine-N-oxide N-allylnormorphine HCl thebaine base
285-286	benzylmorphine base
286	cryptopine base ethylmorphine base dihydromorphine base codeine base
287	morphine base α-monoacetyl-morphine base acetoxyketobemidone HCl
289	racemethorphan base
289-290	cotarnine base
290-291	protopine base
291	narcotine base narcotine HCl
292	*dl*-methadone HCl *d*-methadone HCl *l*-methadone HCl phenadoxone HCl
295-296	*dl*-methadone base *d*-methadone base *l*-methadone base
296	isomethadone HCl pipidone HCl phenadoxone base
298	morphothebaine HCl
299	isomethadone base pipidone base
300	thebenine HCl
303	meconic acid
307	hydrastinine Cl
309-310	dioxyline H_3PO_4 narcotine base
311	papaverine HCl
313	narcotine HCl
314	papaverine base
319-320	thebenine HCl
327	papaverine base
329-330	thebenine HCl
331	cotarnine base—water cotarnine base—water + HCl
332-335	cotarnine base—ethanol + HCl
335	dioxyline H_3PO_4
335-336	cotarnine base—ethanol

spectrum is irregular with three main peaks. The pyrahexyl spectrum is a smooth curve with two maxima. Like the spectrum of phenanthrene (7) the pyrahexyl spectrum has a peak at about 280 mμ., but unlike the phenanthrene spectrum, it has much higher ε values.

ARYL SPECTRA

A. *Aryl carboxylic acids*

Two examples of this group were studied. Opianic acid is a substituted benzoic acid containing, in addition to the COOH group, a formyl and two methoxy groups.

The spectra of benzoic acid (figure 3) and its derivatives, opianic acid (figure 4) and o-acetoxybenzoic acid (aspirin) (8), are different in most respects. However, both opianic and benzoic acids have spectra with a peak at 230 mμ while o-acetoxybenzoic acid and benzoic acid both have a peak at 275 mμ. It should be noted that the spectrum of cocaine base (figure 5) is identical with that of benzoic acid, which in other words is the chromophore of the alkaloid.

B. *Aryl piperidines*

There were eleven compounds in this subgroup whose spectra were obtained. These compounds can be combined into three main sub-subgroups. The first contains cocaine and ecgonine which are quite different chemically from the remaining compounds. Ecgonine is a nonaryl modified piperidine which forms part of the cocaine molecule. The second subgroup contains the piperidine carboxylates; pethidine, ethyl pethidine, α and β prodine and hydroxypethidine, which unlike all others carries a phenol hydroxyl. This subgroup can be further chemically divided into pethidines which are esters of isonipecotic acid, and α and β prodines which are piperidol esters of propionic acid. The third group contains four compounds, all arylpiperidylalkanones, i.e., ketobemidones. The ketobemidones are structurally related, the variation being in the alkyl portion of the ketone, e.g., methyl-, ethyl- and propyl-ketobemidones. Acetoxyketobemidone, in addition to being an ethyl ketone, contains an acetoxy substituent on the aryl ring. The important change in this compound is from a phenol to an ester.

The spectra fall into three groups which relate to the structures in the chemical classes. The spectra of ecgonine (figure 6) and cocaine (figure 5) show maxima at 274 mμ. but are not otherwise closely related. The spectrum of cocaine base has one more peak than the spectrum of the HCl salt, resembling the curve of benzoic acid (figure 3) more than that of ecgonine (*loc. cit.*). The spectra of the aryl piperidine esters, e.g., pethidine (figure 7) and prodine (figures 9 and 10), are characterized by one absorption region consisting of fine structure between 253-264 mμ. and by very low ε values. The spectra of compounds in this group most closely resemble that of benzene (9), with the exception of pethidine (figure 11). The spectrum of this compound is closely related to that of o-cyclohexylphenol (10) and to the spectra of methyl-, ethyl- and propylketobemidone (figures 12, 13, 14) which are all phenols. These compounds have one absorption band showing a maximum in the range 277-280 mμ. The spectrum of acetoxyketobemidone (figure 15) is entirely different from the spectrum of the parent compound, with two maxima at 271 mμ. and 286 mμ.

C. *Diarylalkoneamines*

There were four compounds studied in this group which may be further subdivided into hexanone amines, e.g. pipidone and isomethadone, and heptoneamines, e.g. methadone and phenadoxone. Another compound, α-methadyl acetate, was included. Except for the latter, they are all ketones, α-methadyl acetate being an acetyl ester derived from methadone. All the compounds in this class have two phenyl groups and a variety of substituted amino groups, e.g. dimethylamino, piperidino, and morpholino.

The spectra of the diarylalkoneamines fall into two groups. The first, including isomethadone (figure 16), pipidone (figure 17), methadone (figure 18) and phenadoxone (figure 19) is characterized by two regions of absorption: fine structure between 253-264 mμ and a large single band between 292-299 mμ. The heptanone bases absorb at 299 mμ. and their HCl salts at 296 mμ. The hexanone bases absorb between 295-296 mμ. and their HCl salts at 292 mμ. The *d* and *l* optical isomers of methadone have spectra similar to that of the *dl* form. The ε values of the salts are lower than those of the bases and range from 510-600 for the salts and from 610-880 for the bases at the maximum wave-length of 259 mμ. The second group includes isomers of α-methadyl acetate (figure 20). The spectra of the isomers of α-methadyl acetate (figure 20). The spectra of the *d*-, *l*- and *dl*-isomers are similar. Slight but probably insignificant differences in ε maximum of the three isomers are noted. Fine structure in the region 253-264 mμ. (like the first group) was observed. The large single band, observed in the first group between 292-299 mμ., was not obtained in the second group. The spectrum of α-methadyl acetate resembles that of pethidine (figure 7) in this respect, having two peaks and a shoulder in the fine structure region compared with the three definite peaks occurring in the pethidine spectra. The ε values at about 259 mμ. for the methadyl acetates are intermediate between those for pethidine and methadone. The ε range for pethidine is 200-217, for α-methadyl acetate is 422-434, for methadone is 510-600.

D. *Arylethylamines*

There are four compounds in this group, two of which are trimethoxyphenylethylamines, and two of which are aryl-phenyleneethylamines. The latter contain a ketone and carboxylate attached to the aryl ring and also a methylenedioxy substituent on the phenylene ring.

The spectra of these arylethylamines divide into two groups corresponding to the chemical classification. All five spectra (including narceine HCl—figure 23) show a single absorption maxima at 270 mμ. The narceine spectra (figure 23) have a broad band compared with a

narrower band for the mescaline spectra (figure 21). The ϵ values for the two groups are completely different; that of mescaline base appears to be about 750 and that of narceine base about 9620 at the maxima 270 mμ. The solvent and pH appear to have considerable effect on the spectra of these compounds. The spectrum of mescaline sulphate in 80 per cent ethanol obtained by Salomon and Binà (11) does not compare with ours (figure 21).

ISOQUINOLINE SPECTRA

There are three main subdivisions in this group, dihydro-, phthalide-, and benzylisoquinolines.

A. *Dihydroisoquinolines*

There were two compounds studied in this subgroup, cotarnine and hydrastinine, which differ only in the presence of a methoxyl group on the benzene ring in cotarnine. For a discussion of the structure of these two compounds, see Small (12).

The spectra of these compounds are of the same shape, (comparing the cotarnine base in water + HCl (figure 25) and the hydrastinine chloride in water (figure 26)) with two main bands whose maxima are at 255 mμ. and 331 mμ. for cotarnine and 249 mμ and 307 mμ. for hydrastinine chloride. The hypsochromic shift should be noted. The ϵ values are higher for hydrastinine at the first maxima and higher for cotarnine at the second maxima. The spectra of cotarnine vary with different solvents and pH conditions.

B. *Phthalideisoquinolines*

Only narcotine and narcotine HCl were studied. These compounds are also of the dihydroisoquinoline type, but contain in addition a phthalide substituent.

The spectrum of narcotine and its HCl salt (figure 27) are different from those of the previous group. The spectrum of the HCl salt shows higher *E* values than that of the base, both having peaks at approximately 209 mμ., 291 mμ. and 309-310 mμ.

C. *Benzylisoquinolines*

There are three distinct sub-groups represented in the six compounds studied in this series; papaverine, papaverine. HCl and dioxyline-H_3PO_4 represent the true benzylisoquinolines. Laudanine differs in that the nitrogen containing ring is saturated and there is an OH group on the benzene ring. Cryptopine and protopine are distinctly different and belong in a group by themselves as they contain ten membered rings. The chemistry of cryptopine and protopine has been discussed by Small (13). Dioxyline has an ethoxyl group on the benzyl ring and a methyl group on the isoquinoline ring, while papaverine has a methoxyl group on the benzyl ring. Cryptopine and protopine differ only in that the former has a dimethoxy and the latter a methylenedioxy group substituted on the phenyl ring.

The spectra of the benzylisoquinoline compounds divide into three distinctly different groups. Those of papaverine (figure 28) and dioxyline (figure 29) are similar in shape and in position of maxima and ϵ values. The spectrum of laudanine (figure 30) is quite different to that of papaverine, resembling that of ketobemidone (figure 13), with a single peak at 283 mμ. and lack of fine structure. The spectra of cryptopine (figure 31) and protopine (figure 32) are different from each other except that both have a peak about 290 mμ. The ϵ values are 5880 and 9270 for cryptopine and protopine respectively.

PHENANTHRENE SPECTRA

A. *Phenanthroisoquinolines*

The two compounds studied having the phenanthroisoquinoline nucleus were apomorphine HCl and morphothebaine HCl. The former has two phenol groups on one benzene ring. The latter has two phenolic hydroxyl groups on non-adjacent benzene rings and also a methoxyl group adjacent to one of the phenol hydroxyls. The 8-9 carbon bond in the phenanthrene ring system is saturated. Both compounds have an iminoethano ring.

The spectra of apomorphine HCl (figure 33) and morphothebaine HCl (figure 34) are similar, having absorption maxima in the region 272-276 mμ. The morphothebaine HCl spectrum has two peaks, one at 268 mμ. and the other at 276 mμ. The spectrum of apomorphine HCl shows a single maximum at 272 mμ. The morphothebaine spectrum has a peak at 298 mμ. In this region the apomorphine spectrum is a plateau. The literature spectra reported by Elvidge (14) and Kitasato (15) for apomorphine in this region show fine structure (probably accounted for by an instrument with higher dispersion, e.g., Hilger).

B. *Phenanthroethanoamines*

Thebenine is the only true phenanthrene derivative in this homologous series, the remaining compounds being more fully hydrogenated. It has in addition on the A ring an OCH_3 group and a phenolic hydroxyl in ortho position, and on the C ring a phenolic hydroxide in a position para to the ethylmethylamine group.

The spectrum of thebenine HCl (figure 35) resembles the phenanthrene spectrum (16) more closely than any of the other phenanthrene type narcotic spectra. It has five peaks compared with eleven for phenanthrene. The major peak in the phenanthrene spectrum occurs at 252 mμ. compared with 251 mμ. in the thebenine HCl spectrum. The fine structure in the region 300-350 mμ. is modified in the thebenine HCl spectrum.

C. *Iminoethanophenanthrenes*

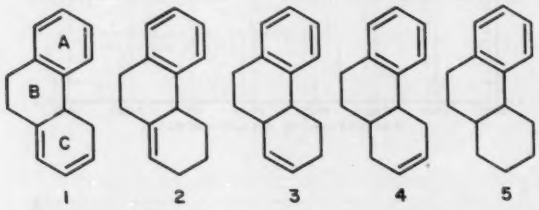
This group consists of eight compounds, seven of which are optical isomers or derivatives of morphan. The remaining compound, sinomenine, is closely related in basic structure; however it has considerably more unsaturation and substituents, e.g. methoxyl, hydroxyl, and carbonyl groups. The methorphans have a methoxy in place of the hydroxyl of the morphans. Compared with sinomenine, the morphinan homologues (i.e., 3-hydroxy-

and 3-methoxy-N-methylmorphinans) have completely saturated B and C rings.

The spectra divide into two groups corresponding to the chemical classification. The morphinan spectra (figures 36 and 37) are characterized by one m. in band extending from 250 mμ. to 290 mμ. and a definite peak occurring in the region extending from 278 mμ. to 283 mμ. The spectrum of racemethorphan base (figure 37) reveals a peak at 281 mμ. and 289 mμ. respectively. It is characterized by low ε values at the minima. The ε values of the minima in this series vary between isomers and are the lowest observed for any narcotic. The highest absorption of the spectra of these compounds is of the order of 9,000 while the lowest is around 20. The second type of spectrum in this group was obtained from a study of sinomenine HCl (figure 38). The spectrum does not appear to be related to any other obtained in this study.

D. *Iminoethanophenanthrofurans*

The majority of common opium alkaloids and their derivatives fall into this group. Eighteen compounds were studied and these can be further chemically subdivided into five groups, depending on the basic structures which are shown in the following diagrams.



In group I : thebaine
group II : neopine
group III: morphine, ethyl-, benzyl-N-allyl-nor-, diacetyl-, α-monoacetylmorphine, pseudomorphine, morphine-N-oxide and codeine
group IV : Acedicone®
group V : dihydromorphine, dihydrocodeine, dihydromorphinone, dihydrocodeinone, methyldihydromorphinone, dihydrohydroxy-codeinone

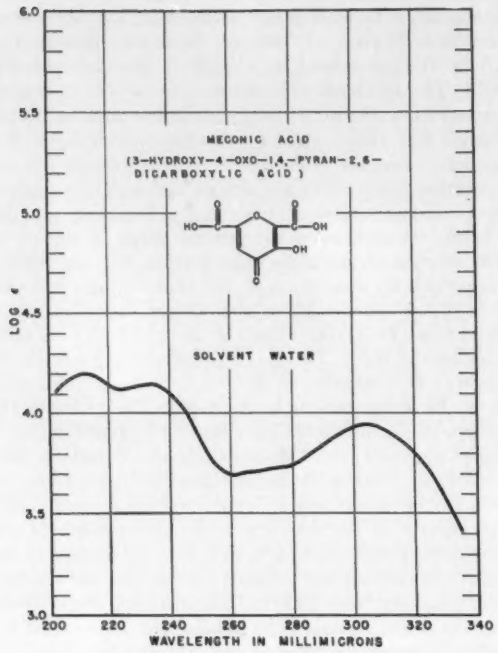
Some of the main structural differences in group III and V are of interest from the spectral point of view. In group III the basic morphine structure is modified by ether or ester formation in cases of ethyl- and benzyl-morphine and diamorphine and α-monoacetyl morphine respectively. In N-allyl normorphine and morphine-N-oxide the methyl group associated with the N-atom in morphine has been substituted by an allyl group or an oxygen atom respectively. Pseudomorphine is believed to be a dimer of morphine. Group V compounds are divided into two groups; the dihydro-morphine and codeine and the keto containing morphine derivatives.

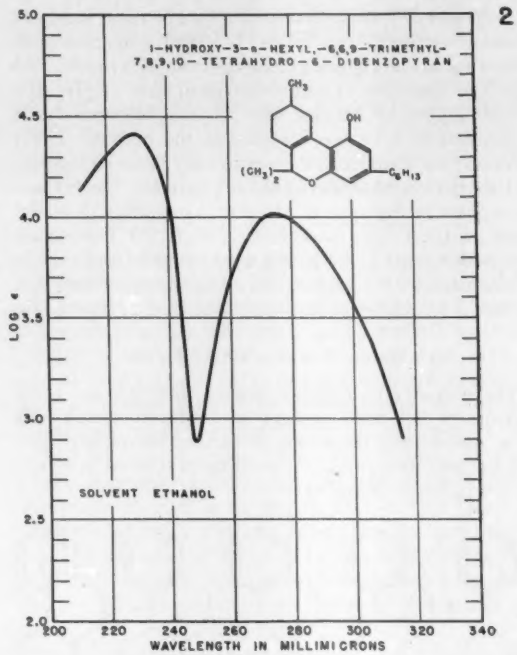
The spectra of the compounds in the five groups will be discussed by comparing the spectra of various members in each groups. Thebaine shows hyperconjugation in the C ring system which affects the absorption of light. The spectrum of thebaine (figure 42) is characterized by a higher ε maximum value than morphine (about five times greater) or dihydromorphine. The spectra of neopine (figure 41), codeine (figure 40) and morphine (figure 39) are almost identical in respect to the position of the absorption maxima and corresponding ε values, as well as in the general shape of the curve. The spectra of morphine salts (figure 39) are similar, except that the absorption of morphine sulphate is double that of the other salts or that of the base because of the presence of two moles of morphine per mole of morphine sulfate. There is no inflection point in the spectra of morphine HI, whereas other morphine salts show this characteristic in the region 230-240 mμ. The spectra of dihydromorphine (figure 43) and dihydrocodeine (figure 44) show absorption from 285-286 mμ. with ε values of 1700, while other morphine derivatives absorb in the same region with ε values of only 1500. The spectra of the ethers of morphine, e.g. ethyl- and benzyl-morphine (figures 49 and 50), are similar to the spectra of codeine and neopine except that the ε values have increased from 1500 to 1600 and 1800 respectively. The spectra of esters of morphine, e.g. mono- and diacetyl morphine (figures 51 and 52) are different. The former spectrum has a maxima at 287 with an ε value of about 1600, while the latter spectrum exhibits a hypsochromic shift to 281 mμ. with an ε value of 1300. The additional acetyl substituent on the alcoholic OH appears to have brought about both a hypo- and hypsochromic effect.

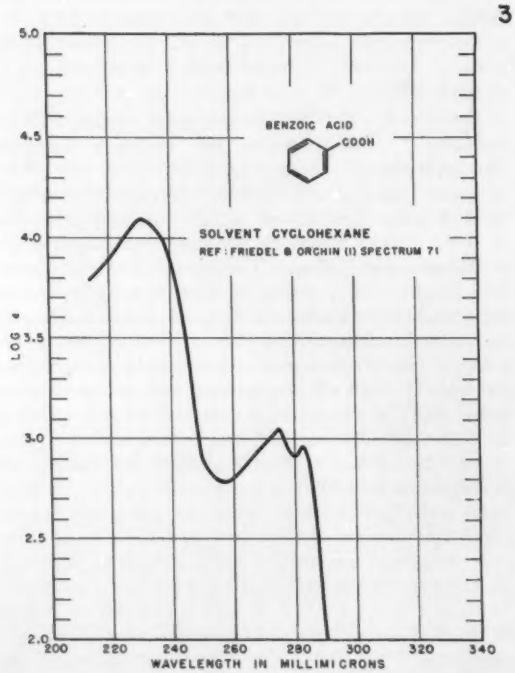
The spectra of N-allyl-normorphine (figure 55) and morphine-N-oxide resemble the morphine spectrum. The spectrum of pseudo-morphine (figure 56) is very different from that of morphine, with a broad absorption band showing a maximum at 229 mμ; and an ε value of about 37,000. There are two inflection points located at 260 mμ. and 282 mμ. The spectrum of Acedicone® HCl (figure 53) is similar to that of morphine except that a slight hypsochromic shift has occurred, locating the maximum of absorption at 280 mμ. The spectra of the group V compounds are characterized by a slight hypo and hypsochromic effect compared with the spectrum of morphine. The absorption maxima of the salts occur in the region 280-282 mμ. and have corresponding ε values of 1210 to 1250. The spectra all have inflection points in the region 230-240 mμ.

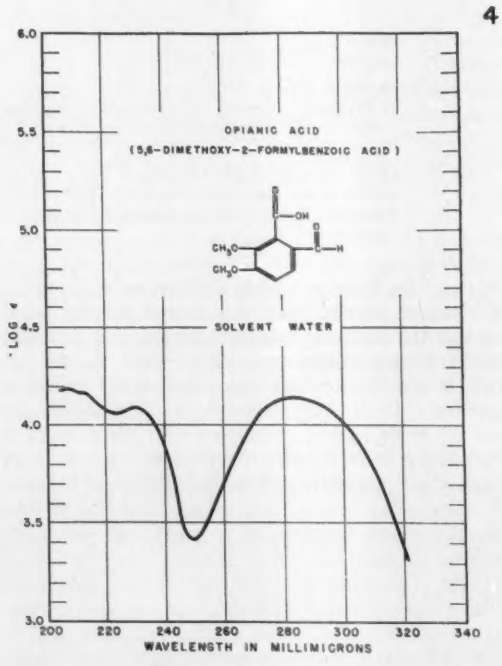
Atlas of Ultraviolet Absorption Spectra of Narcotics and Related Alkaloids

Figures 1-4

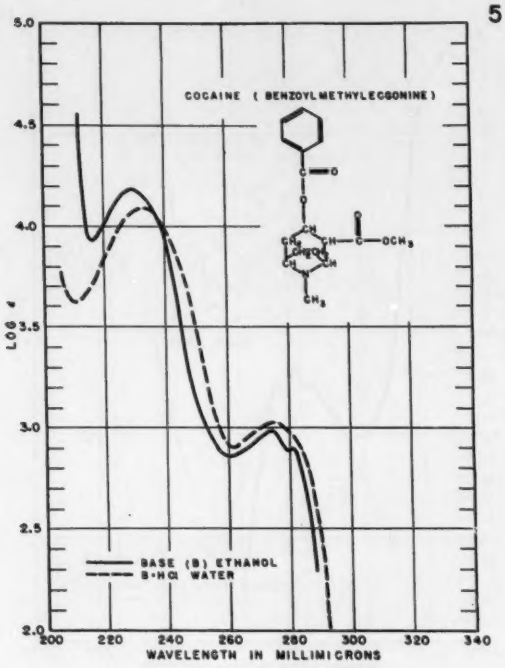


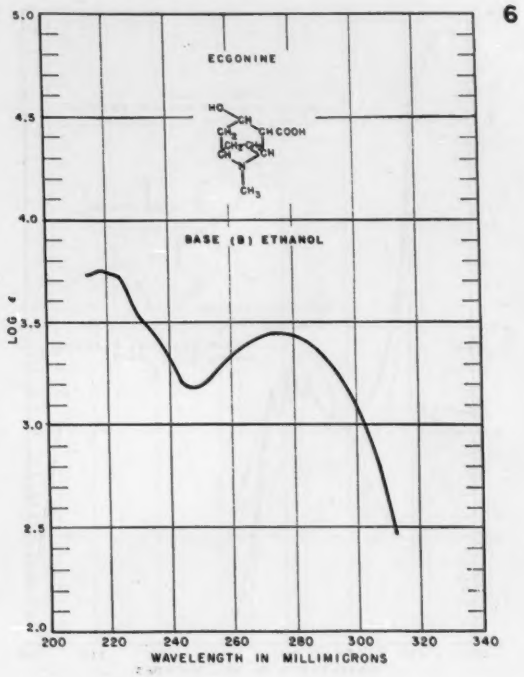


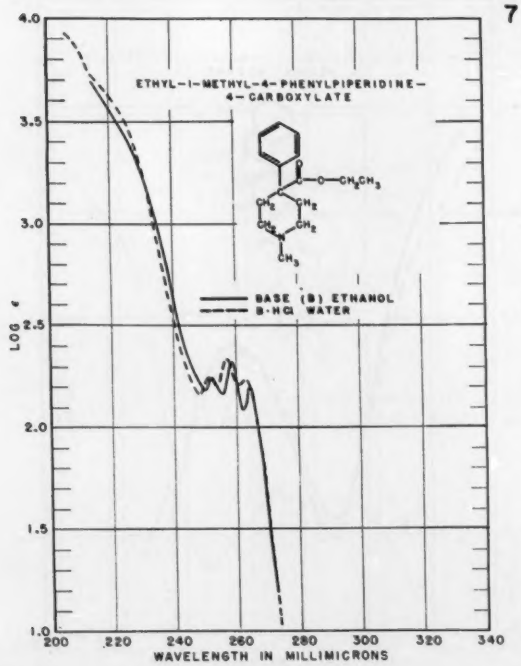


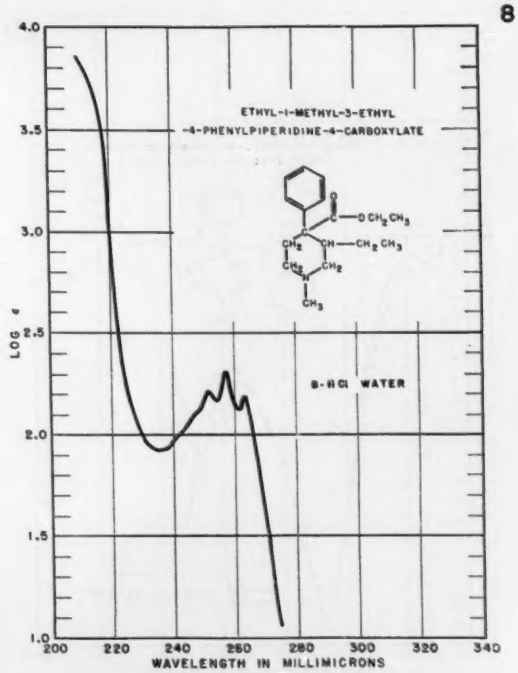


FIGURES 5-8


5
COCAINE (BENZOYLMETHYLECGONINE)
BASE (B) ETHANOL
B·HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS


6
ECGONINE
BASE (B) ETHANOL
LOG ε
WAVELENGTH IN MILLIMICRONS


7
ETHYL-1-METHYL-4-PHENYLPIPERIDINE-4-CARBOXYLATE
BASE (B) ETHANOL
B·HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS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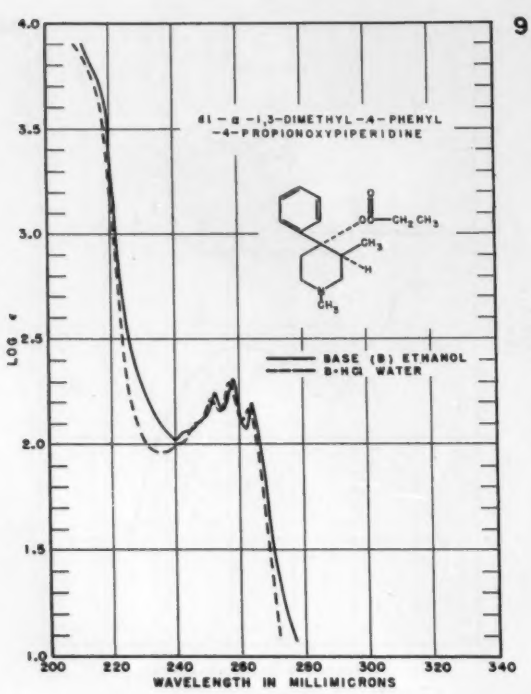
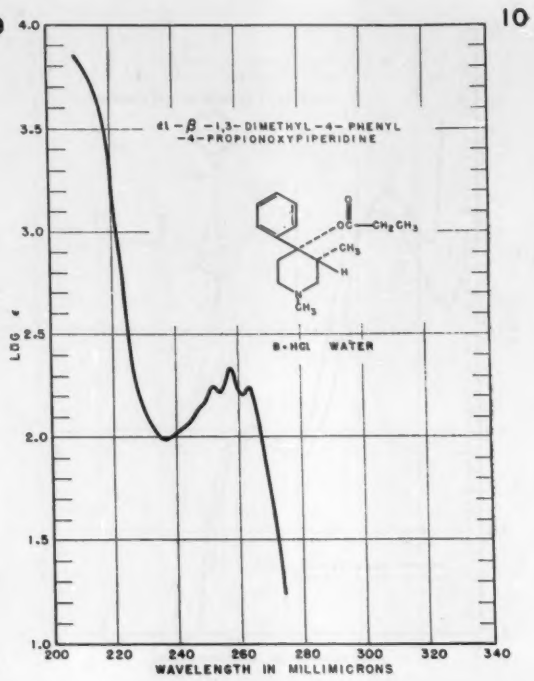
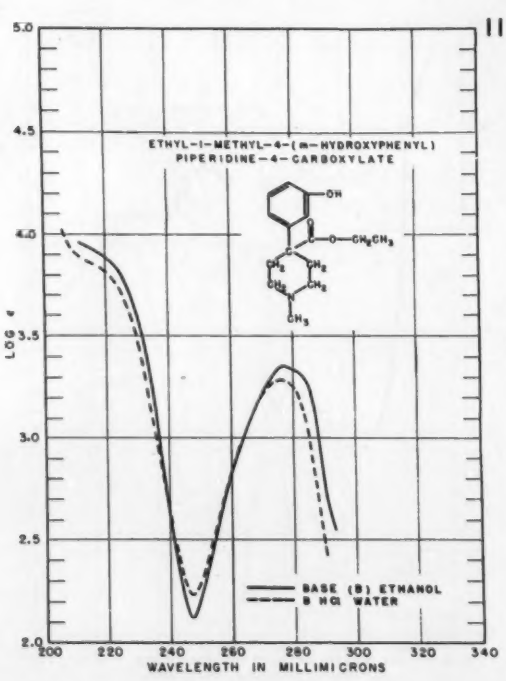
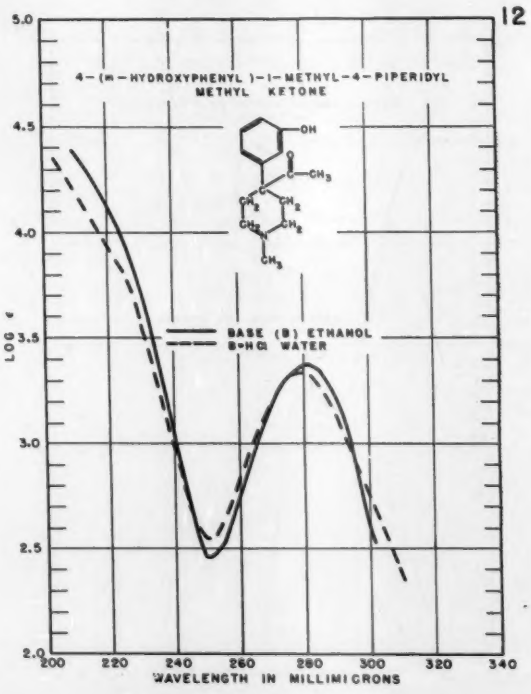
ETHYL-1-METHYL-3-ETHYL-4-PHENYLPIPERIDINE-4-CARBOXYLATE
B·HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS

FIGURES 9-12

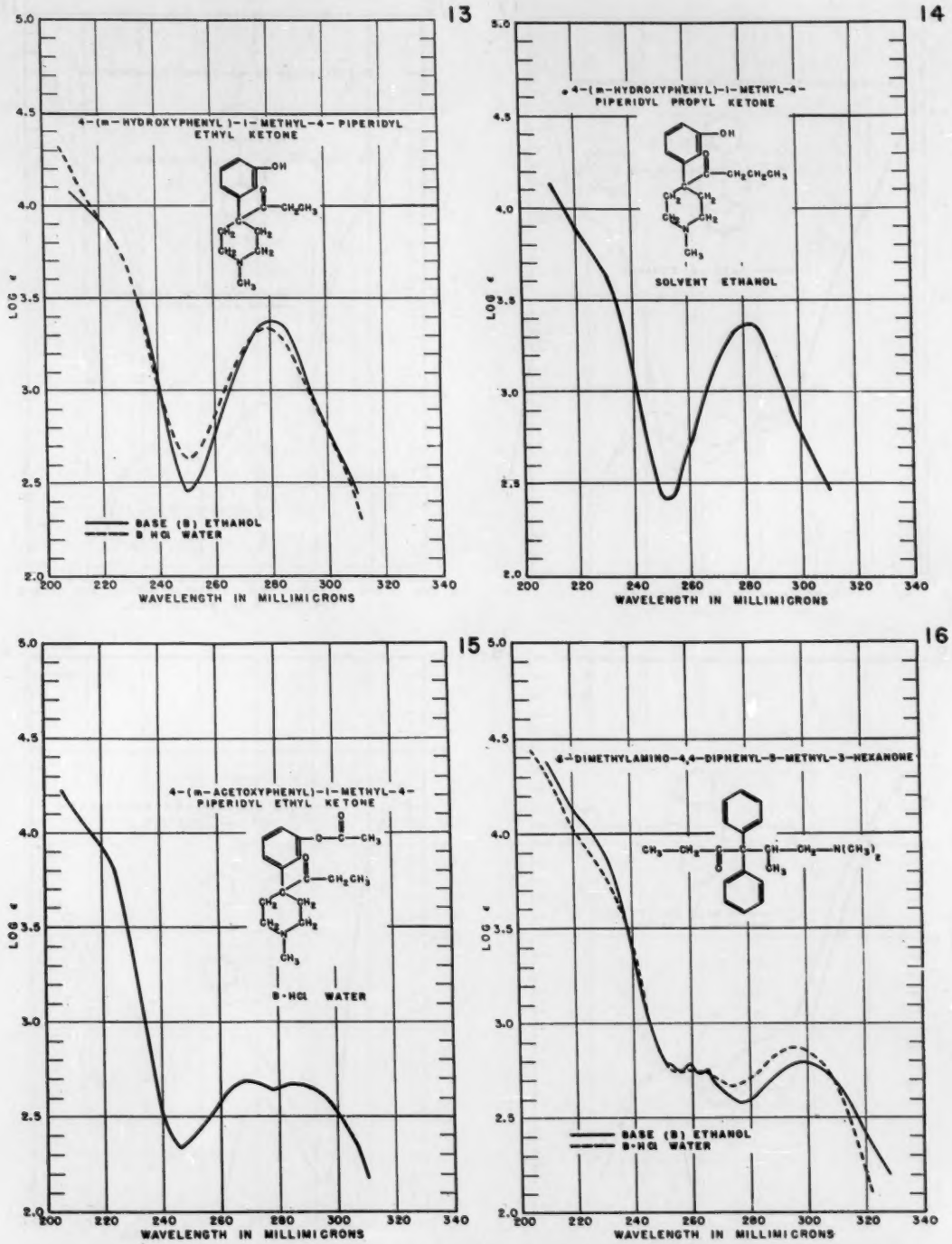

9
dl – α –1,3–DIMETHYL–4– PHENYL
–4–PROPIONOXYPIPERIDINE
BASE (B) ETHANOL
B•HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS


10
dl – β –1,3– DIMETHYL –4– PHENYL
–4–PROPIONOXYPIPERIDINE
B•HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS

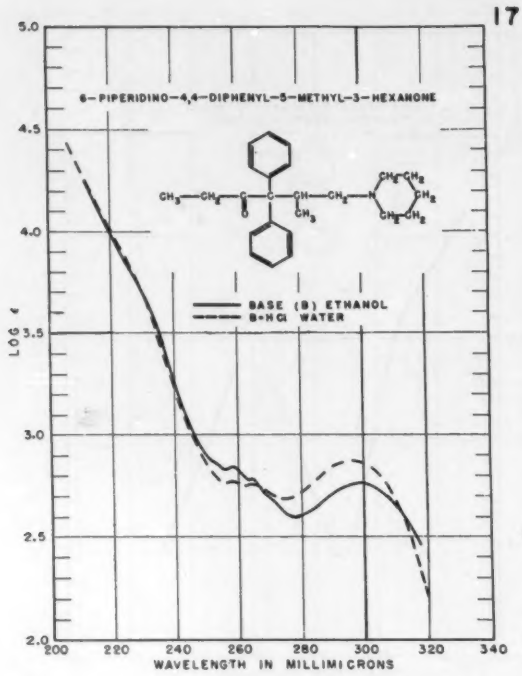

11
ETHYL–1–METHYL–4–(m–HYDROXYPHENYL)
PIPERIDINE–4– CARBOXYLATE
BASE (B) ETHANOL
B HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS

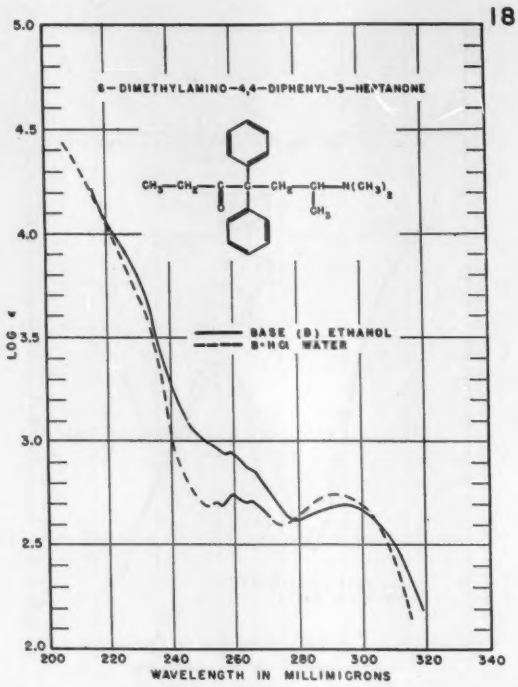

12
4–(m–HYDROXYPHENYL)–1–METHYL–4– PIPERIDYL
METHYL KETONE
BASE (B) ETHANOL
B•HCl WATER
LOG ε
WAVELENGTH IN MILLIMICRONS

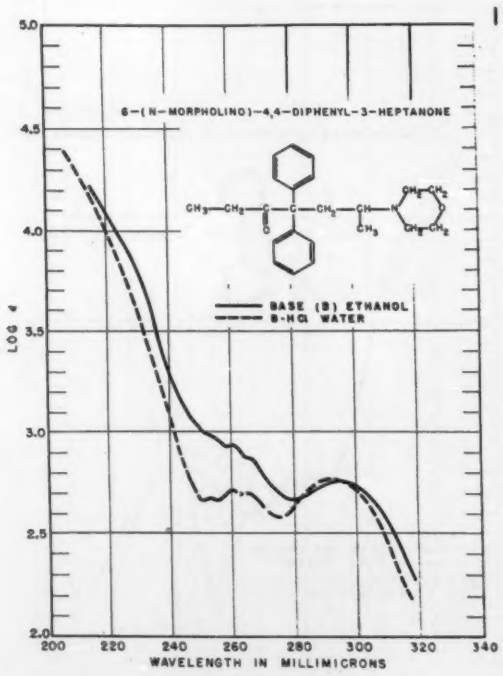
FIGURES 13-16

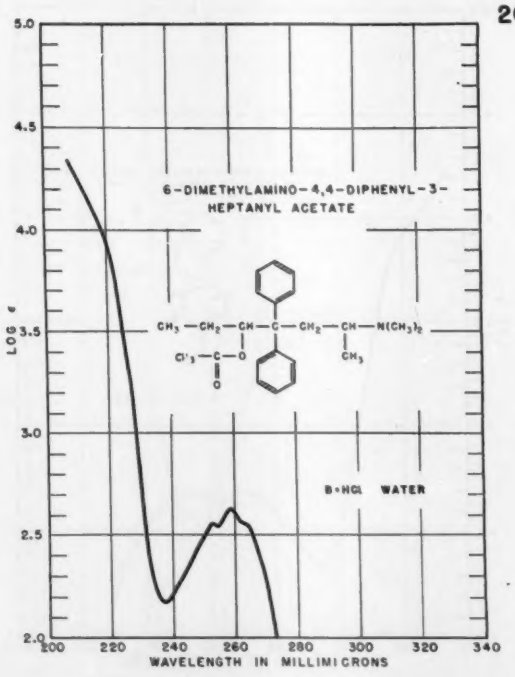


FIGURES 17-20



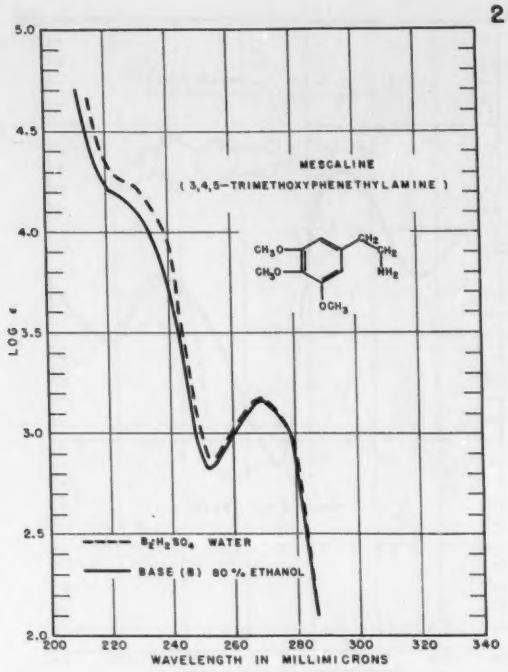






FIGURES 21-24

21



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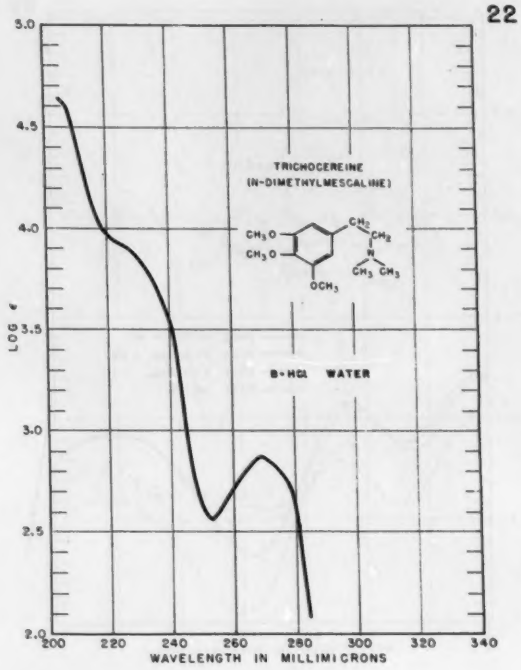

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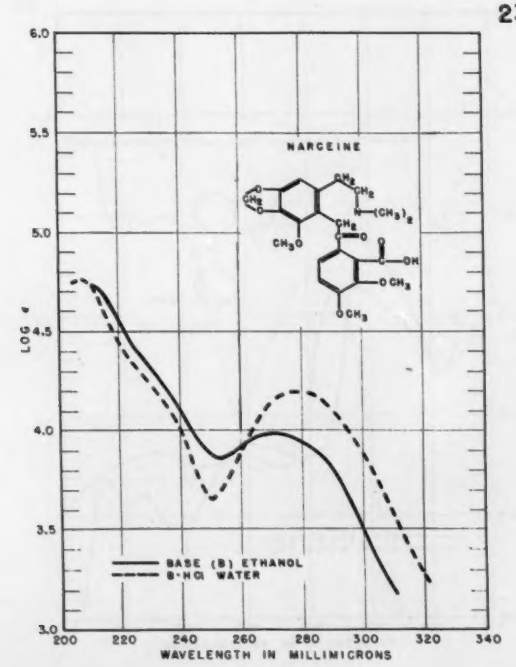

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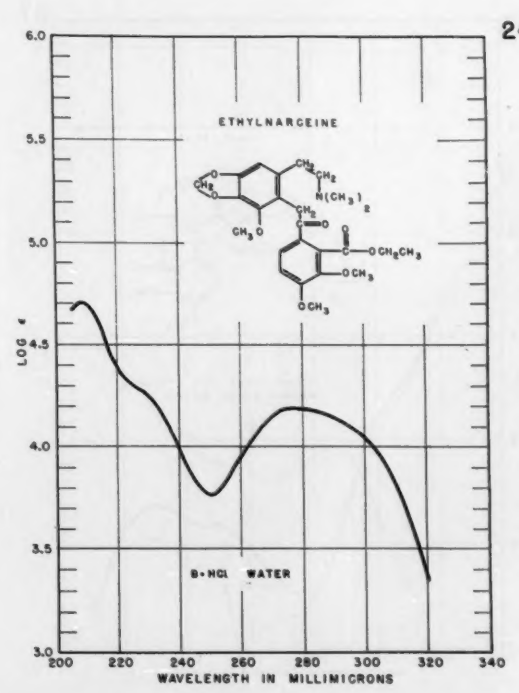
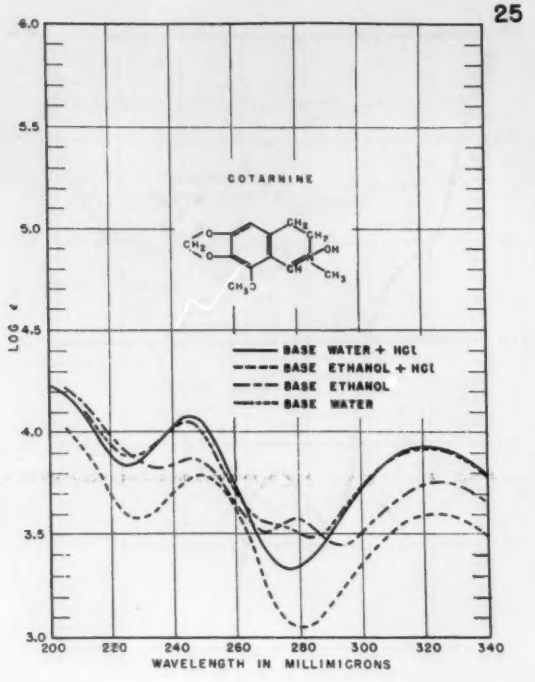
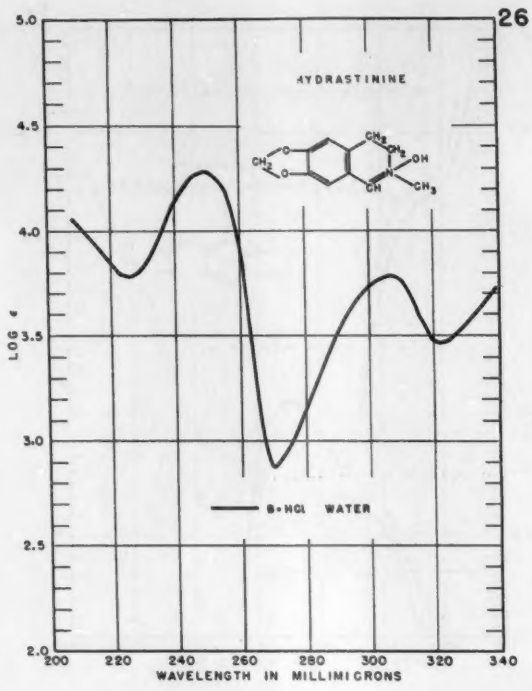
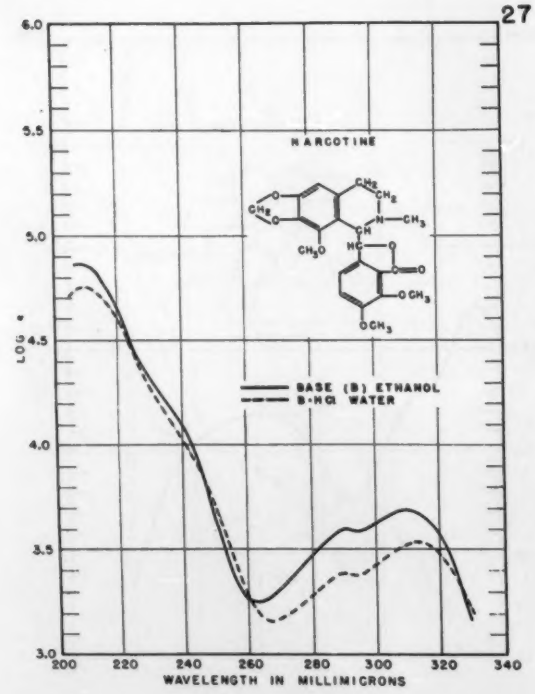
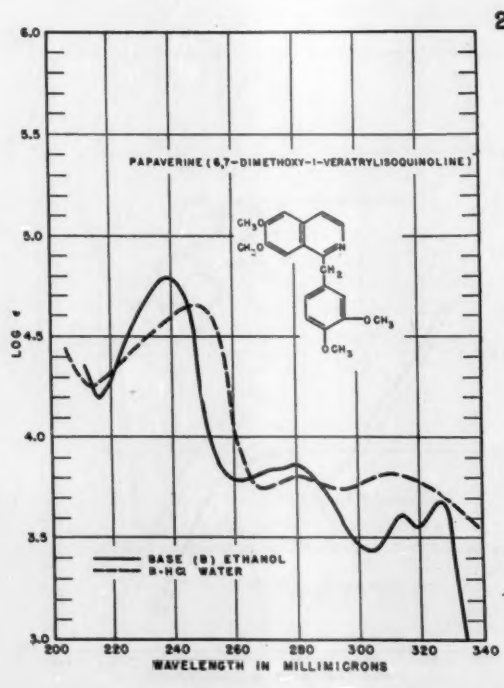


FIGURES 25-28

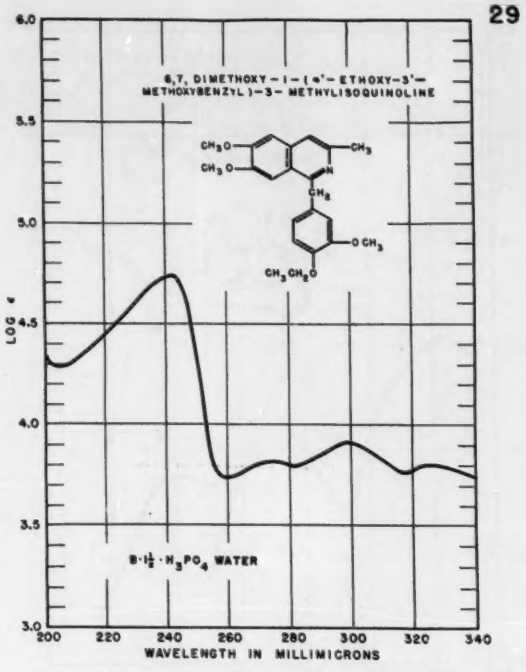


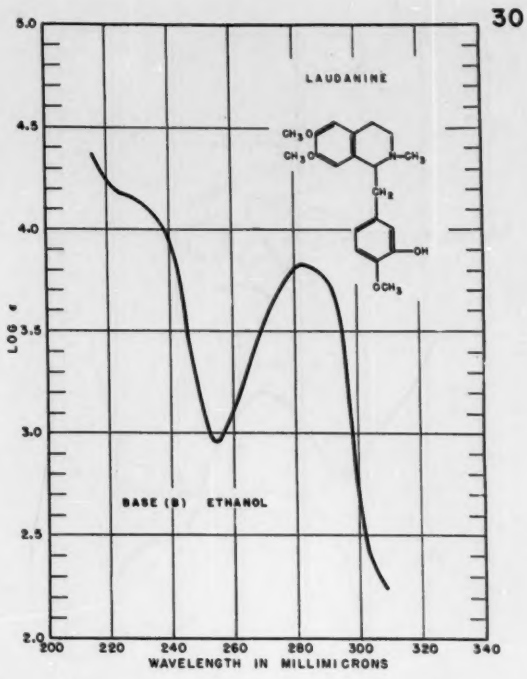


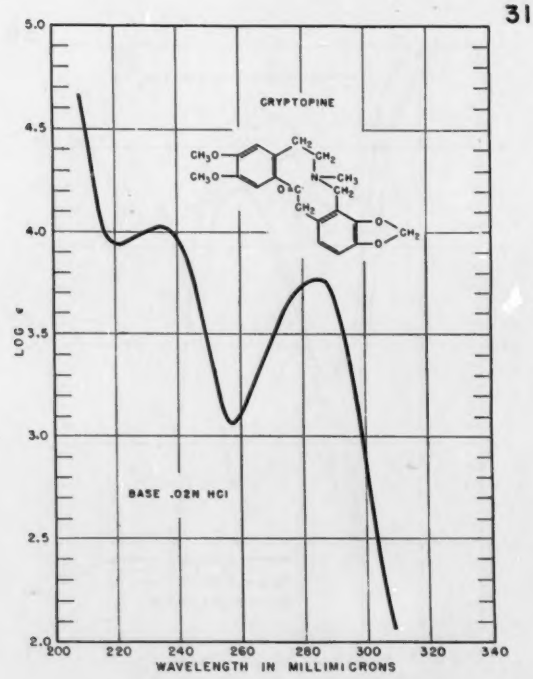


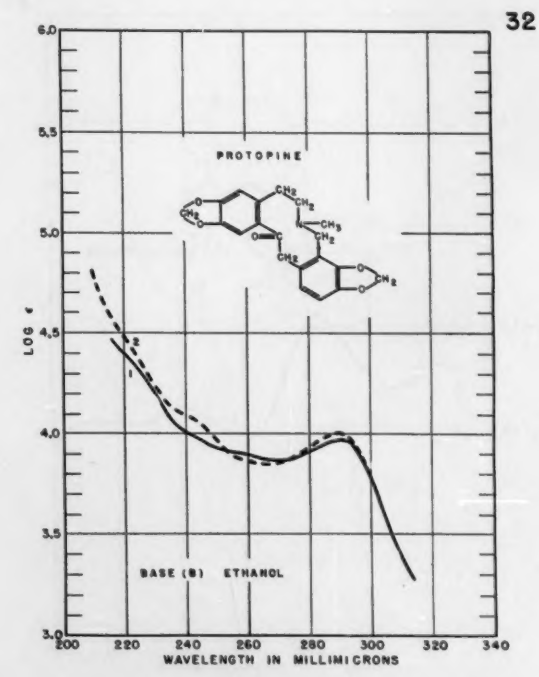


FIGURES 29-32

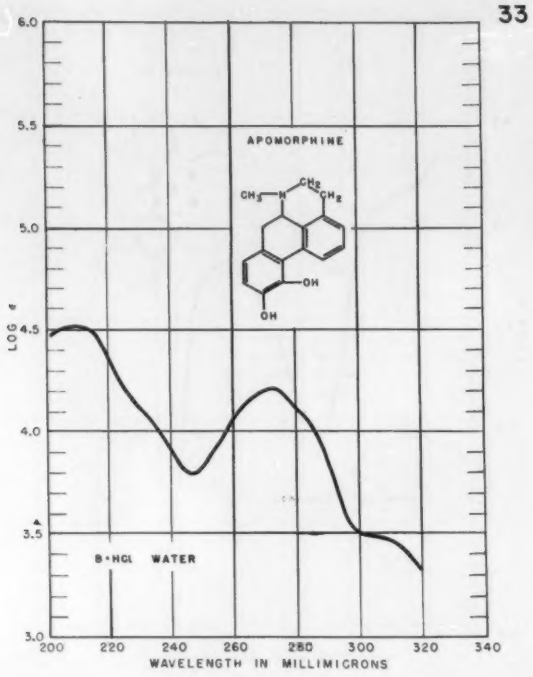


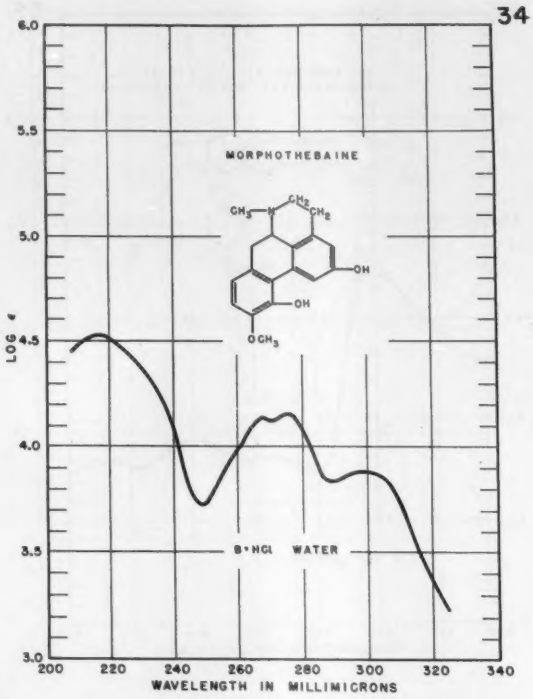


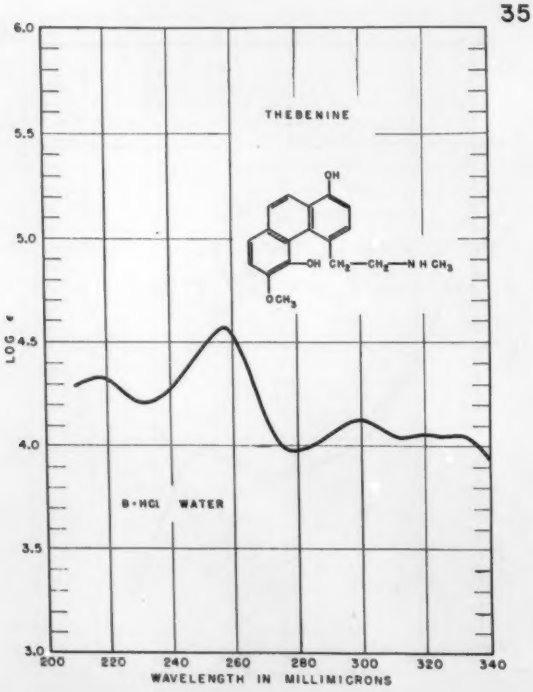


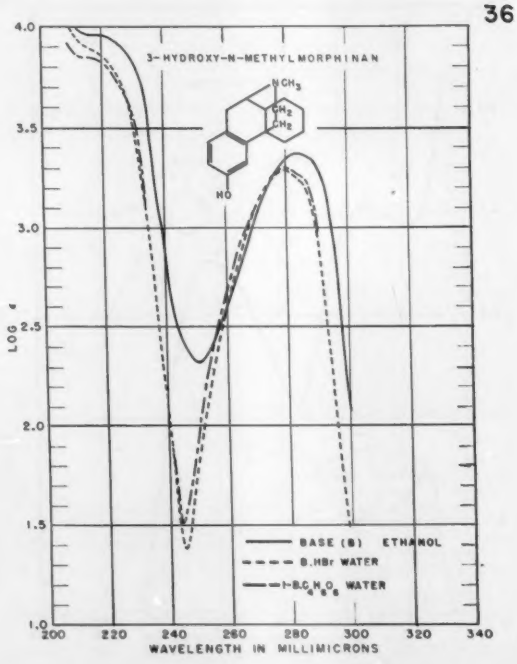


FIGURES 33-36

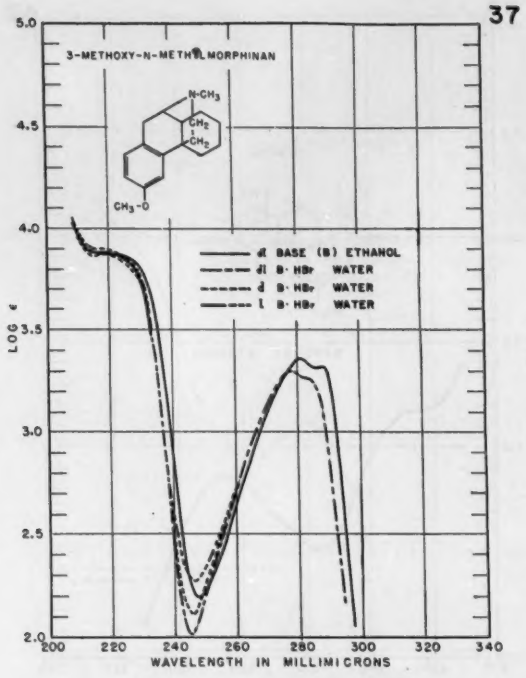


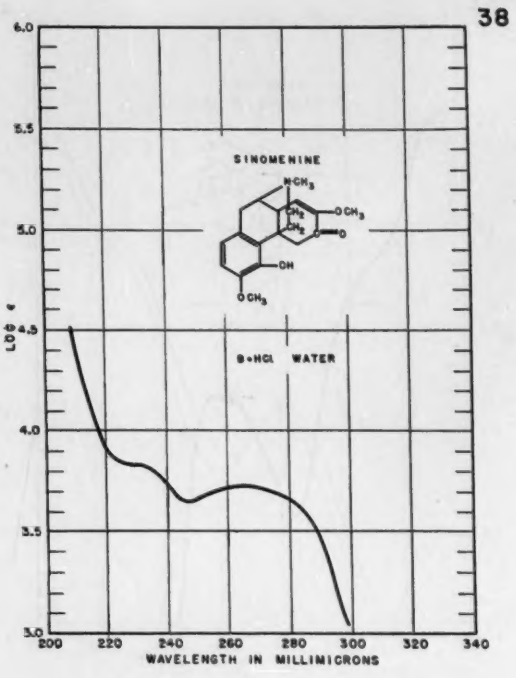


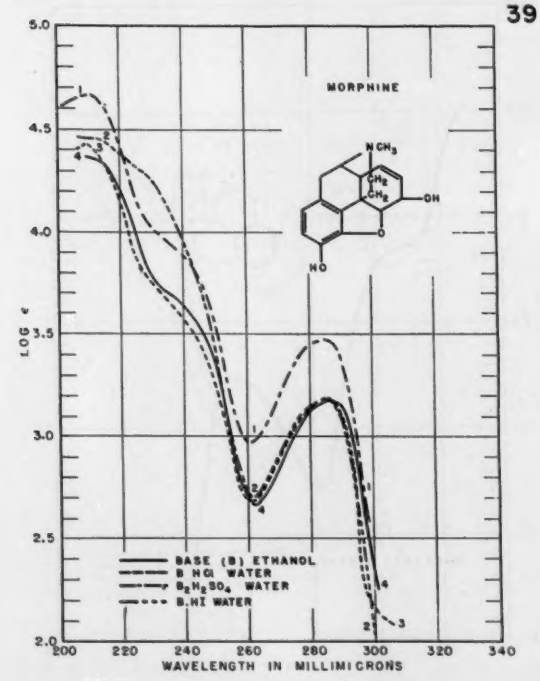


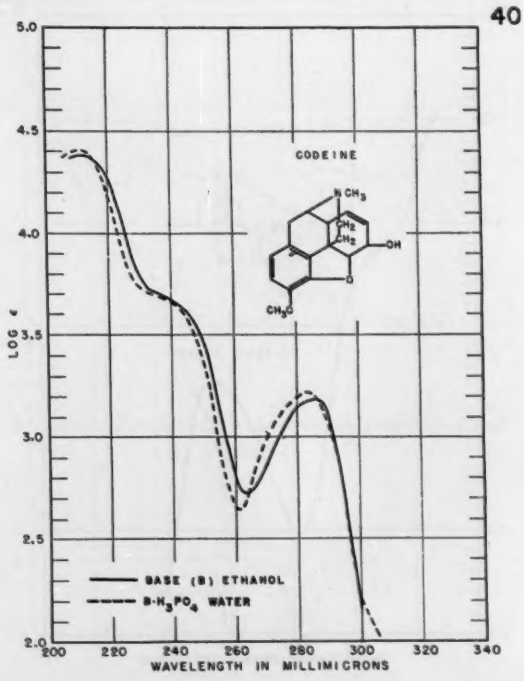


FIGURES 37-40

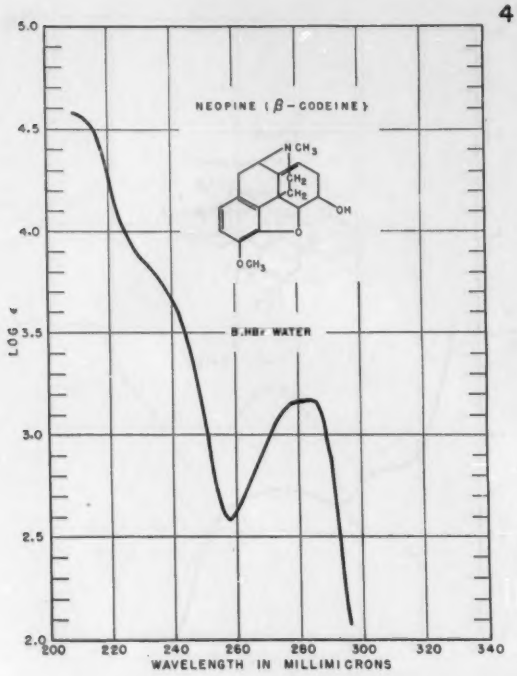


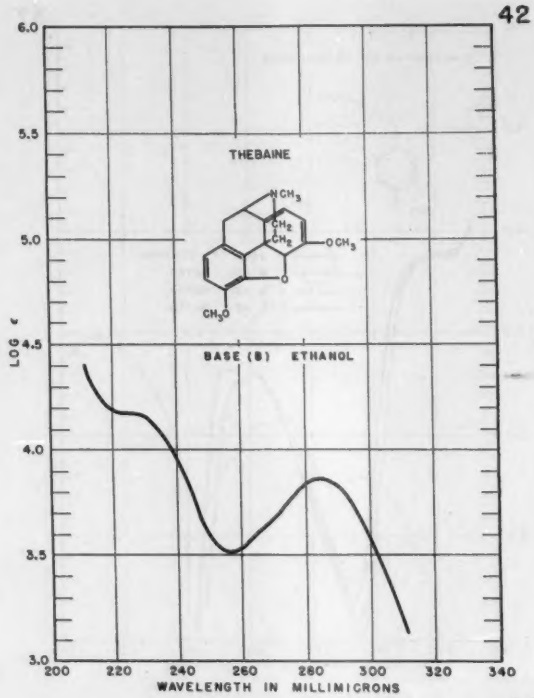


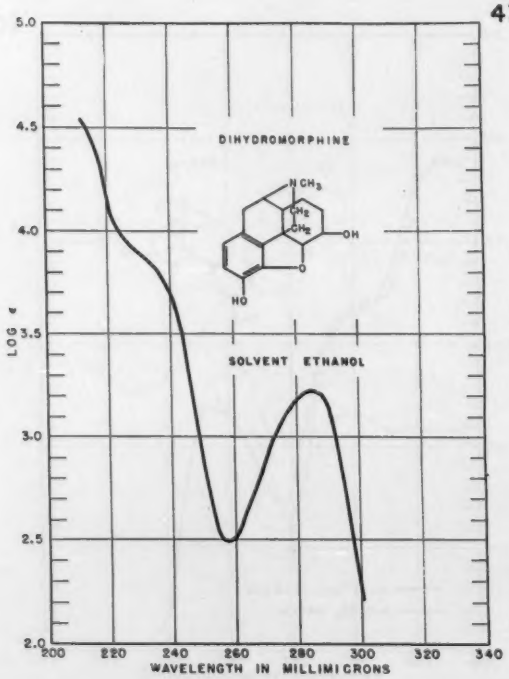


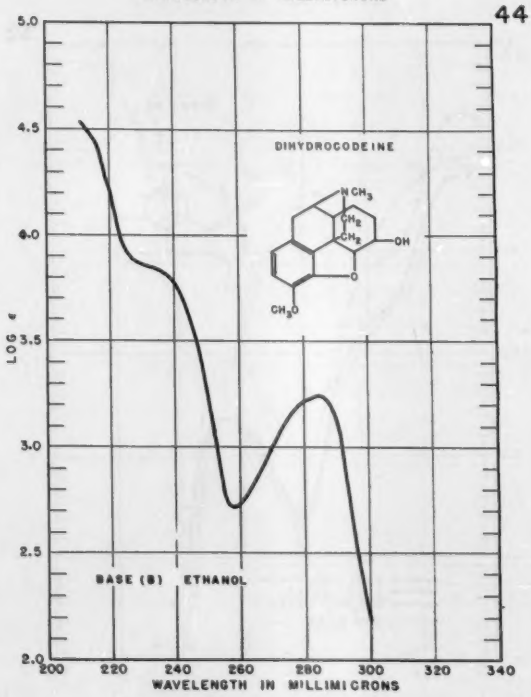


FIGURES 41-44

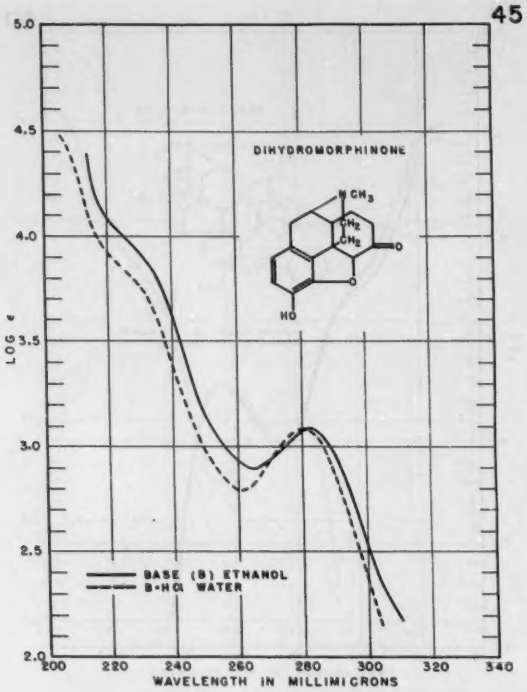


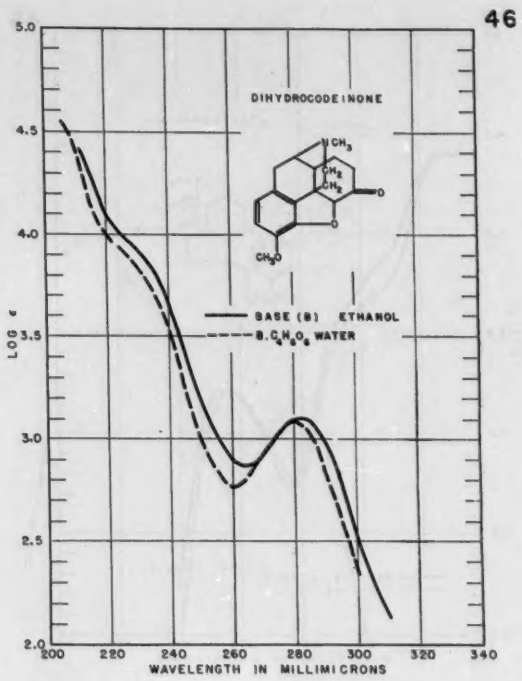


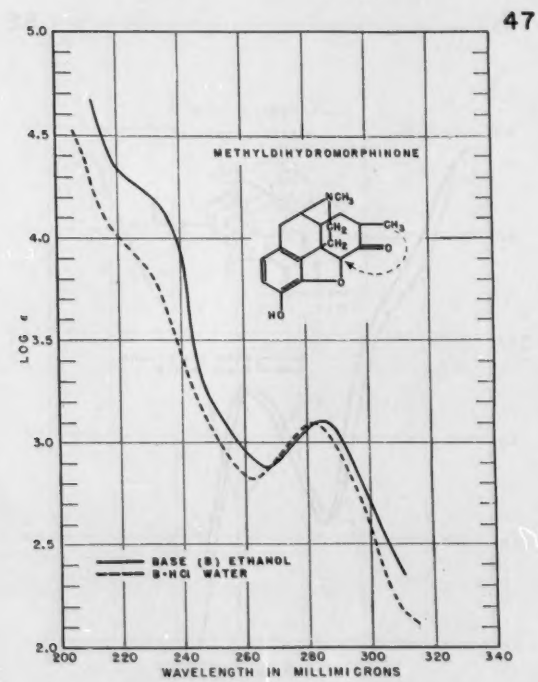


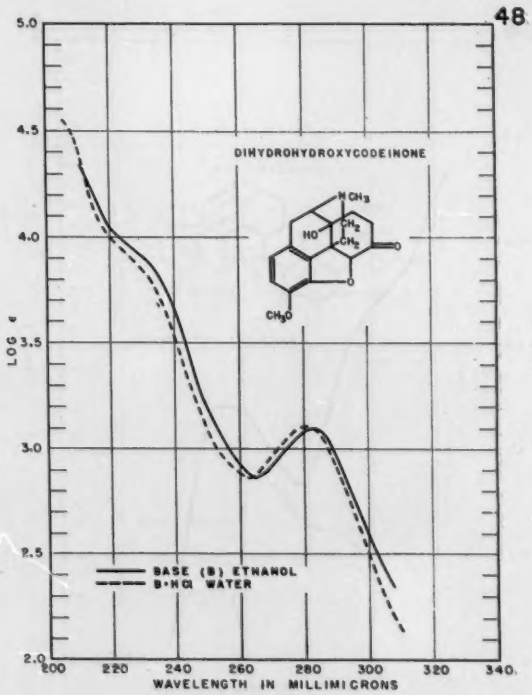


FIGURES 45-48

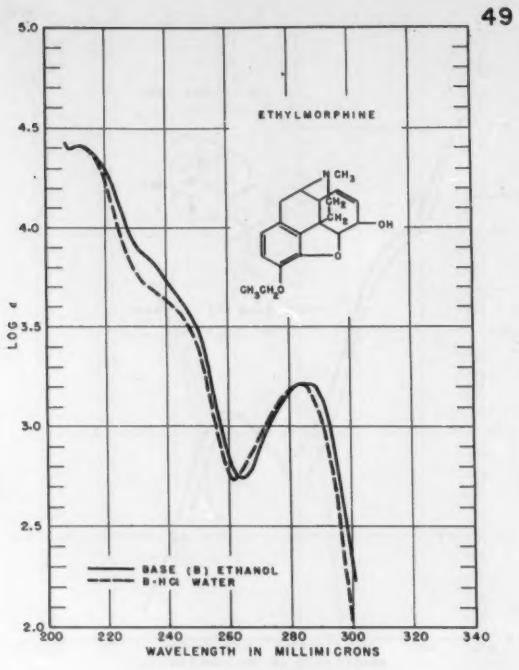


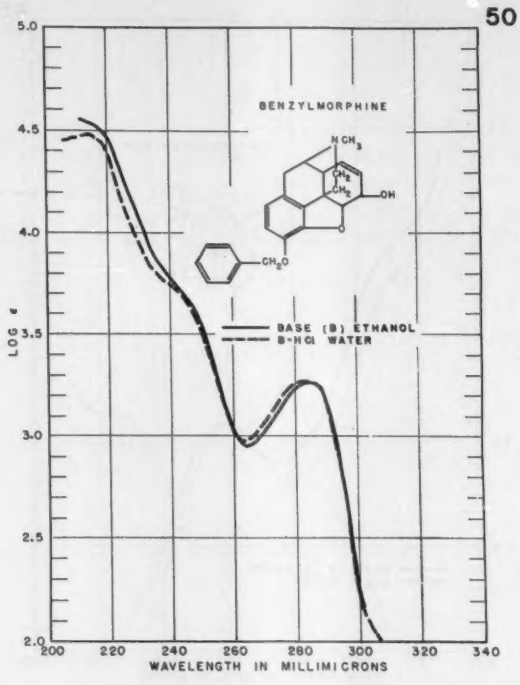


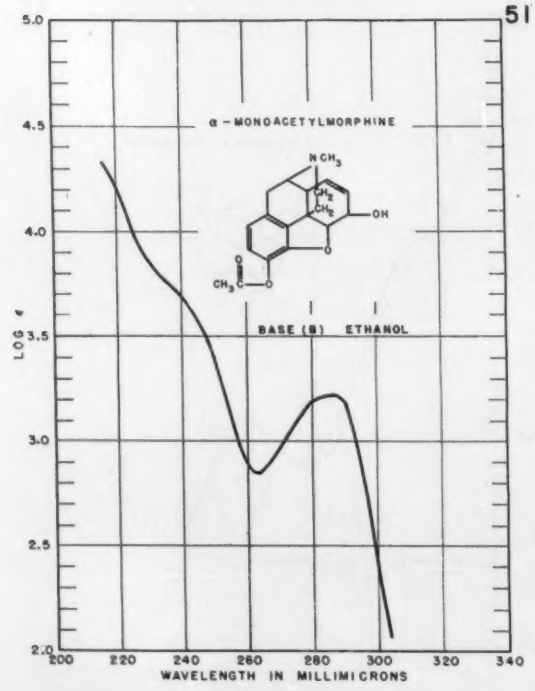


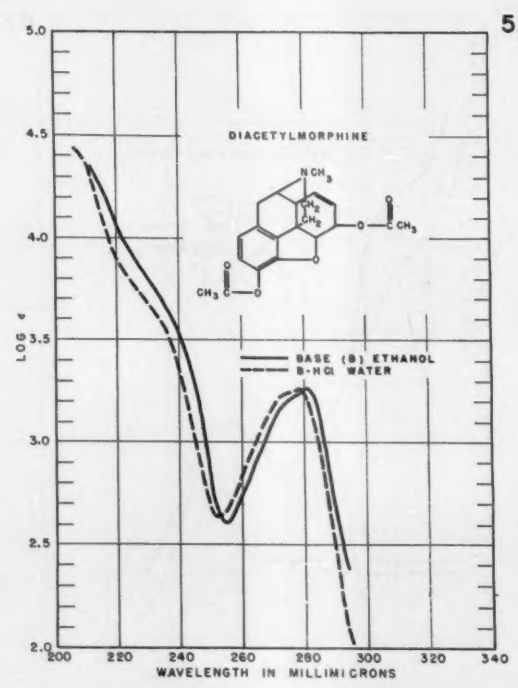


FIGURES 49-52









FIGURES 53-56

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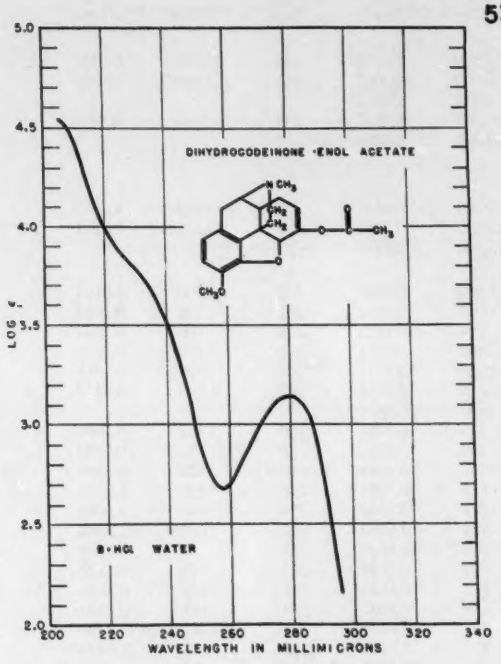

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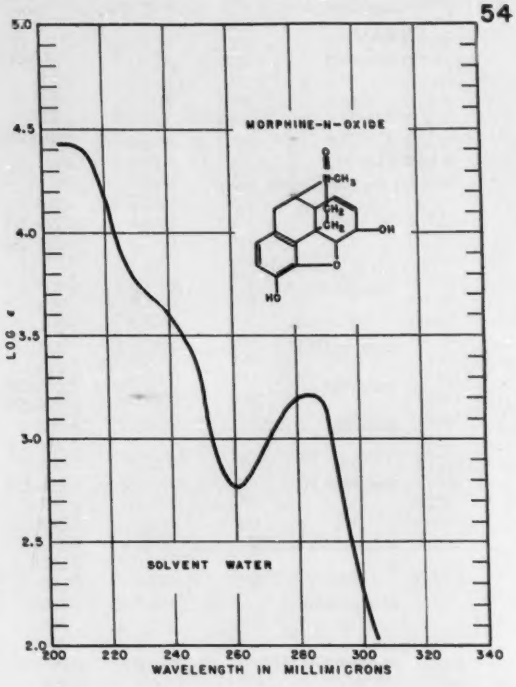

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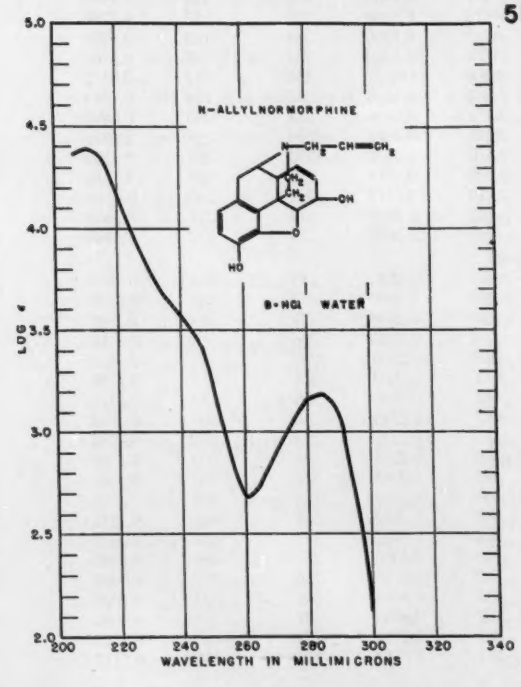

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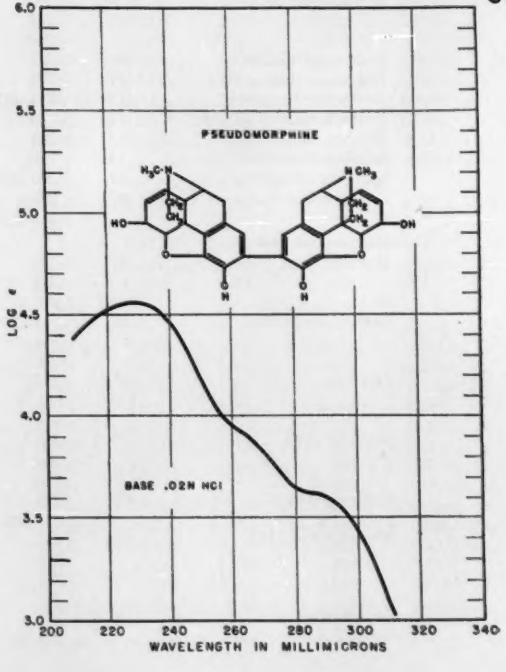

Table II

SPECTRAL DATA FOR NARCOTIC IDENTIFICATION ARRANGED ACCORDING TO CHEMICAL FAMILIES

Compound	*No.*	λ *Max.* (mμ)	ε *Max.*	*Conc.* (g./l.)	λ *Min.* (mμ)	ε *Min.*	*Conc.* (g./l.)
1. PYRANS							
meconic acid	1	210-211	15,500	0.0107	224	12,800	0.0107
		234	14,300	0.0107	261	5,000	0.0107
		303	8,810	0.0107			
pyrahexyl	2	229	26,200	0.0057	249	710	0.0204
		276-277	10,200	0.0204			
2. ARYLS							
(a) *Aryl carboxylic acids*							
opianic acid	4	209	15,400	0.0101	225	11,500	0.0101
		229-231	12,300	0.0101	250	2,580	0.0101
		282-284	13,800	0.0101			
(b) *Aryl piperidines*							
cocaine	5	230	15,600	0.0103	216	8,390	0.0103
		274	977	0.1032	261	720	0.1032
		281	794	0.1032	279	760	0.1032
cocaine.HCl	5	233	12,400	0.0101	211	4,200	0.0101
		274	1,060	0.2515	261	790	0.2515
ecgonine	6	218-219	5,610	0.0186	247	1,500	0.0372
		274-275	2,800	0.0372			
pethidine	7	252	176	0.5080	250	152	0.5080
		258	210	0.5080	255	142	0.5080
		264	157	0.5080	262	120	0.5080
pethidine.HCl	7	251-252	176	0.5080	248	147	0.5080
		257	217	0.5080	254	160	0.5080
		263	174	0.5080	261	160	0.5080
ethylpethidine.HCl	8	251	165	0.5120	235	83	0.5120
		257	201	0.5120	254	148	0.5120
		263	152	0.5120	261	132	0.5120
dl-α-prodine	9	252	171	0.5400	240	105	0.5400
		258	207	0.5400	255	142	0.5400
		264	154	0.5400	262	118	0.5400
dl-α-prodine.HCl	9	251	168	0.4960	236	92	0.4960
		257	203	0.4960	254	142	0.4960
		263	151	0.4960	261	130	0.4960
dl-α-prodine.HCl	10	252	175	0.5200	237	97	0.5200
		257	212	0.5200	254	162	0.5200
		263	172	0.5200	261	158	0.5200
hydroxypethidine	11	277	2,260	0.0527	248	132	0.0527
hydroxypethidine.HCl	11	275	1,960	0.1010	247	172	0.1010
methylketobemidone	12	281-282	2,350	0.0496	252	250	0.0496
methylketobemidone.HCl	12	280	2,070	0.1016	250	355	0.1016
ketobemidone	13	281	2,370	0.0500	250	285	0.0500
ketobemidone.HCl	13	280	2,270	0.1016	251	435	0.1016
propylketobemidone	14	280-282	2,320	0.0512	252	260	0.0512
acetoxyketobemidone.HCl	15	271	482	0.2468	247	217	0.2468
		285-286	465	0.2468	278	439	0.2468
(c) *Diarylalkoneamines*							
isomethadone	16	259	608	0.2800	256	562	0.2800
		265	561	0.2800	263	540	0.2800
		299	620	0.2800	277	380	0.2800
isomethadone.HCl	16	258-259	569	0.2500	256	558	0.2500
		264	565	0.2500	261	560	0.2500
		296	751	0.2500	274	470	0.2500
pipidone	17	259	697	0.2240	256	679	0.2240
		265	612	0.2240	264	600	0.2240
		299	587	0.2240	278	390	0.2240
pipidone.HCl	17	258	599	0.2505	256	590	0.2505
		264	585	0.2505	262	570	0.2505
		296	759	0.2505	274	490	0.2505
dl-methadone	18	259	883	0.2032	258	860	0.2032
		295-296	486	0.2032	279	419	0.2032
dl-methadone.HCl	18	253	499	0.5080	251	480	0.5080
		259	542	0.5080	256	492	0.5080
		264	513	0.5080	263	500	0.5080
		292	557	0.5080	274	390	0.5080
d-methadone	18	259	861	0.2112	258	840	0.2112
		295-296	474	0.2112	279	405	0.2112

Table II (cont.)

Compound	No.	λ Max. (mμ)	ε Max.	Conc. (g./l.)	λ Min. (mμ)	ε Min.	Conc. (g./l.)
d-methadone.HCl	18	253	478	0.5050	251	465	0.5050
		259	529	0.5050	256	468	0.5050
		265	505	0.5050	263	490	0.5050
		292	553	0.5050	274	379	0.5050
l-methadone	18	259	866	0.2224	258	870	0.2224
		295-296	478	0.2224	280	425	0.2224
l-methadone.HCl	18	253	491	0.5040	250	480	0.5040
		259	540	0.5040	256	480	0.5040
		264	521	0.5040	262	500	0.5040
		292	557	0.5040	275	380	0.5040
phenadoxone	19	259-260	861	0.2032	258	850	0.2032
		296	570	0.2032	279	462	0.2032
phenadoxone.HCl	19	253	465	0.2580	251	448	0.2580
		259	513	0.2580	256	448	0.2580
		265	495	0.2580	263	485	0.2580
		292	581	0.2560	275	378	0.2580
dl-α-methadyl acetate.HCl	20	253	363	0.5240	237	150	0.5240
		258	432	0.5240	255	350	0.5240
d-α-methadyl acetate.HCl	20	253	365	0.5000	238	155	0.5000
		258	434	0.5000	255	350	0.5000
l-α-methadyl acetate.HCl	20	253	355	0.4920	238	158	0.4920
		258	422	0.4920	255	345	0.4920
(d) *Arylethylamines*							
mescaline.H_2SO_4—water	21	269	1,470	0.2240	252	680	0.2240
80 per cent ethanol	21	269	1,480	0.1300	254	739	0.1300
trichocereine.HCl	22	269	756	0.2780	253	365	0.2780
narceine	23	270	9,620	0.0203	252	7,300	0.0203
narceine.HCl	23	208	56,900	0.0040	250	4,530	0.0203
		277	15,500	0.0203			
ethylnarceine.HCl	24	208-209	51,100	0.0041	250	5,800	0.0202
		277-278	15,500	0.0198			
3. ISOQUINOLINES							
(a) *Dihydroisoquinolines*							
cotarnine—water	25	254-255	11,400	0.0094	237	7,700	0.0094
		331	8,460	0.0094	294	3,100	0.0094
100 per cent ethanol	25	255-256	7,450	0.0206	246	6,800	0.0206
		289-290	3,830	0.0206	279	3,250	0.0206
		335-336	5,690	0.0206	304	2,820	0.0206
water+HCl	25	255	12,100	0.0094	236	6,900	0.0094
		330-332	8,490	0.0094	287	2,150	0.0094
100 per cent ethanol+HCl	25	258-259	6,220	0.0206	240	3,850	0.0206
		332-335	4,040	0.0206	292	1,150	0.0206
hydrastinine chloride	26	249	20,500	0.0042	225	6,100	0.0042
		307	6,690	0.0208	270	760	0.0208
					323	2,920	0.0208
(b) *Phthalideisoquinolines*							
narcotine	27	209	73,500	0.0020	263	1,800	0.0758
		291	4,020	0.0758	294	3,900	0.0758
		309-310	4,910	0.0758			
narcotine.HCl	27	211	58,000	0.0051	268	1,450	0.0510
		291	2,520	0.0510	294	2,420	0.0510
		313	3,510	0.0510			
(c) *Benzylisoquinolines*							
papaverine	28	239	68,200	0.0047	215	21,000	0.0047
		279-280	7,170	0.0311	261	5,900	0.0311
		314	3,990	0.0311	305	2,650	0.0311
		327	4,720	0.0311	319	3,450	0.0311
papaverine.HCl	28	249-250	48,900	0.0067	214	17,900	0.0067
		280-282	6,360	0.0134	269	5,500	0.0134
		311	6,590	0.0134	294	5,420	0.0134
dioxyline.H_3PO_4	29	252	56,400	0.0040	215	19,000	0.0040
		284-285	6,470	0.0202	270	5,350	0.0202
		309-310	7,950	0.0202	292	6,180	0.0202
		335	6,230	0.0202	327	5,800	0.0202
dl-laudanine	30	283	6,800	0.0240	255	900	0.0240
cryptopine	31	234	10,700	0.0166	222	8,800	0.0166
		286	5,880	0.0416	258	1,180	0.0416
protopine	32(1)	290-291	9,270	0.0204	272	7,320	0.0204
	(2)	290-291	10,100	0.0200	266	7,080	0.0200

Table II *(cont.)*

Compound	No.	λ Max. (mμ)	ε Max.	Conc. (g./l.)	λ Min. (mμ)	ε Min.	Conc. (g./l.)
4. PHENANTHRENES							
(a) *Phenanthroisoquinolines*							
apomorphine.HCl	33	211	32,400	0.0042	247	6,200	0.0105
		272	16,300	0.0105			
morphothebaine.HCl	34	217	34,200	0.0042	249	5,300	0.0208
		268	13,600	0.0208	271	13,200	0.0208
		276	14,300	0.0208	289	6,850	0.0208
		298	7,650				
(a) *Phenanthroethanoamines*							
thebenine.HCl	35	217-218	21,500	0.0102	231	16,000	0.0102
		257	37,500	0.0102	279	9,400	0.0102
		300	13,400	0.0102	312	11,000	0.0102
		319-320	11,400	0.0102	324	11,000	0.0102
		329-330	11,400	0.0102			
(c) *Iminoethanophenanthrenes*							
racemorphan	36	219	9,000	0.0109	218	9,200	0.0109
		283	2,350	0.0544	251	212	0.0544
racemorphan.HBr	36	279-280	1,900	0.1022	245	23.5	0.1022
levorphan.$C_4H_6O_8$	36	279	2,000	0.1064	244	32.0	0.1064
racemethorphan	37	220-221	7,510	0.0206	218	7,420	0.0206
		281	2,320	0.1032	248	158	0.1032
		289	2,110	0.1032	287	2,050	0.1032
racemethorphan.HBr	37	219	7,740	0.0103	216	7,600	0.0103
		278	2,000	0.1032	245	100	0.1032
dextromethorphan.HBr	37	218	7,560	0.0106	215	7,400	0.0102
		278	2,040	0.1016	246	135	0.1016
levomethorphan.HBr	37	219-220	7,960	0.0106	217	7,850	0.0102
		278	2,010	0.1016	246	192	0.1016
sinomenine.HCl	38	265	5,230	0.0416	248	4,500	0.0416
(d) *Iminoethanophenanthrofurans*							
morphine	39	287	1,510	0.1046	263	465	0.1046
morphine.HCl	39	209	26,200	0.0103	261	490	0.1030
		285	1,540	0.1030			
morphine.HI	39	285	1,510	0.1056	262	515	0.1056
$(morphine)_2H_2SO_4$	39	211	46,400	0.0107	261	930	0.1068
		285	3,000	0.1068			
codeine	40	211-212	24,000	0.0107	263	535	0.1072
		286	1,550	0.1072			
codeine.H_3PO_4	40	212	25,500	0.0102	261	442	0.1010
		284	1,650	0.1010			
neopine.HBr	41	284	1,490	0.1000	258	380	0.1000
thebaine	42	285	7,330	0.0205	256	3,200	0.0205
dihydromorphine	43	286	1,700	0.1008	258	295	0.1008
dihydrocodeine	44	284-285	1,720	0.1016	258	515	0.1016
dihydromorphinone	45	282-283	1,230	0.0976	265	790	0.0976
dihydromorphinone.HCl	45	280	1,220	0.1002	261	625	0.1002
dihydrocodeinone	46	282-283	1,270	0.1040	264	725	0.1040
dihydrocodeinone.$C_4H_6O_8$	46	280	1,220	0.1006	261	582	0.1006
methyldihydromorphinone	47	284-285	1,280	0.0984	267	760	0.0984
methyldihydromorphinone.HCl	47	282	1,250	0.1006	262	670	0.1006
dihydrohydroxycodeinone	48	283	1,250	0.1008	265	730	0.1008
dihydrohydroxycodeinone.HCl	48	280	1,210	0.1010	263	670	0.1010
ethylmorphine	49	286	1,680	0.1000	265	542	0.1000
ethylmorphine.HCl	49	211	26,800	0.0103	208	25,400	0.0103
		283-284	1,610	0.1002	261	530	0.1002
benzylmorphine	50	285-286	1,820	0.1008	265	880	0.1008
benzylmorphine.HCl	50	213	31,600	0.0102	262	950	0.1002
		283-284	1,860	0.1002			
α-monoacetylmorphine	51	287	1,660	0.1008	262	705	0.1008
diamorphine (diacetyl-morphine)	52	281	1,820	0.1000	255	400	0.1000
diamorphine.HCl	52	278	1,800	0.1000	252	430	0.1000
Acedicon®.HCl	53	280	1,410	0.1006	258	485	0.1006
morphine-N-oxide	54	209	27,700	0.0052	260	570	0.0516
		285	1,630	0.0516			
N-allyl-normorphine.HCl	55	209-211	24,200	0.0101	260	483	0.1010
		285	1,520	0.1010			
pseudomorphine	56	222-20	36,700	0.085	—	—	—

Indexes

(a) *Name index for ultraviolet spectra of narcotics and related compounds*

This index includes alphabetically the common names and the chemical names of the compounds studied. The number following the name refers to the number of its spectrum. More than one common name is given for some compounds. The chemical name is listed showing the fundamental structure first, followed by the substituents, thus 5,6-dimethoxy-2-formylbenzoic acid is listed under b; benzoic acid, 5,6-dimethoxy-2-formyl.

(b) *Formula index for spectra*

The formulae are listed in increasing order of C atoms, followed in turn by increasing order of H, N, and O atoms. The number of the spectrum is listed after the chemical name.

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Formula index for spectra

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$C_{10}H_{10}O_5$ 5,6-dimethoxy-2-formylbenzoic acid, 4.
$C_{11}H_{12}NO_2Cl.H_2O$ hydrastinine chloride monohydrate, 26.
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$C_{14}H_{19}NO_2.HCl$ 4-(m-hydroxyphenyl)-1-methyl-4-piperidyl methyl ketone hydrochloride, 12.
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$C_{15}H_{21}NO_2$ 4-(m-hydroxyphenyl)-1-methyl-4-piperidyl ethyl ketone, 13.
$C_{15}H_{21}NO_2.HCl$ ethyl-1-methyl-4-phenylpiperidine-4-carboxylate hydrochloride, 7.
$C_{15}H_{21}NO_2.HCl$ 4-(m-hydroxyphenyl)-1-methyl-4-piperidyl ethyl ketone hydrochloride, 13
$C_{16}H_{23}NO_3$ ethyl-1-methyl-4-(m-hydroxyphenyl)-piperidine-4-carboxylate, 11.
$C_{16}H_{23}NO_3.HCl$ ethyl-1-methyl-4-(m-hydroxyphenyl)-piperidine-4-carboxylate hydrochloride, 11.
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$C_{16}H_{23}NO_2$ 4-(m-hydroxyphenyl)-1-methyl-4-piperidyl propyl ketone, 14.
$C_{16}H_{23}NO_2.HCl$ (cis)-*dl*-α-1,3-dimethyl-4-phenyl-4-propionoxy piperidine hydrochloride, 9.
$C_{16}H_{23}NO_2.HCl$ (trans)-*dl*-β-1,3-dimethyl-4-phenyl-4-propionoxy piperidine hydrochloride, 10.
$C_{17}H_{17}NO_3.HCl.1/2H_2O$ apomorphine hydrochloride hemihydrate, 33.
$C_{17}H_{19}NO_2$ dihydromorphinone, 45

$C_{17}H_{19}NO_3.H_2O$	morphine monohydrate, 39.
$C_{17}H_{19}NO_3.HCl.3H_2O$	morphine hydrochloride trihydrate, 39.
$C_{17}H_{19}NO_3.HCl$	dihydromorphinone hydrochloride, 45.
$C_{17}H_{19}NO_3.HI.2H_2O$	morphine hydroiodide dihydrate, 39.
$(C_{17}H_{19}NO_3)_2.H_2SO_4.5H_2O$	morphine sulphate pentahydrate, 39.
$C_{17}H_{19}NO_4$	morphine-*N*-oxide, 54.
$C_{17}H_{21}NO_3.H_2O$	dihydromorphine monohydrate, 43.
$C_{17}H_{21}NO_4$	benzoylmethyl ecgonine, 5.
$C_{17}H_{21}NO_4.HCl$	benzoylmethyl ecgonine hydrochloride, 5.
$C_{17}H_{23}NO$	*dl*-3-hydroxy-N-methylmorphinan, 36.
$C_{17}H_{23}NO.HBr.1/2H_2O$	*dl*-3-hydroxy-N-methylmorphinan hydrobromide hemihydrate, 36.
$C_{17}H_{23}NO.C_4H_6O_6.2H_2O$	*l*-3-hydroxy-N-methylmorphinan tartrate dihydrate, 36.
$C_{17}H_{23}NO_3.HCl$	4-(m-acetoxyphenyl)-1-methyl-4-piperidyl ethyl ketone hydrochloride, 15.
$C_{17}H_{25}NO_2.HCl$	ethyl-1-methyl-3-ethyl-4-phenylpiperidine-4-carboxylate hydrochloride, 8.
$C_{18}H_{19}NO_3.HCl$	morphothebaine hydrochloride, 34.
$C_{18}H_{19}NO_3.HCl.H_2O$	thebenine hydrochloride monohydrate, 35.
$C_{18}H_{21}NO_3$	codeine, 40
$C_{18}H_{21}NO_3$	dihydrocodeinone, 46.
$C_{18}H_{21}NO_3.HBr$	neopine hydrobromide, 41.
$C_{18}H_{21}NO_3.2H_2O(?)$	methyldihydromorphinone dihydrate (?), 47.
$C_{18}H_{21}NO_3.HCl$	methyldihydromorphinone hydrochloride, 47.
$C_{18}H_{21}NO_3.H_3PO_4.XH_2O$	codeine phosphate mixture of hydrates, 40.
$C_{18}H_{21}NO_3.C_4H_6O_6.2H_2O(?)$	dihydrocodeinone bitartrate dihydrate (?), 46.
$C_{18}H_{21}NO_4$	dihydrohydroxycodeinone, 48.
$C_{18}H_{21}NO_4.HCl.H_2O(?)$	dihydrohydroxycodeinone hydrochloride monohydrate (?), 48.
$C_{18}H_{23}NO_3$	dihydrocodeine, 44.
$C_{18}H_{25}NO$	*dl*-3-methoxy-N-methylmorphinan, 37.
$C_{18}H_{25}NO.HBr.H_2O$	*l*-3-methoxy-N-methylmorphinan hydrobromide monohydrate, 37.
$C_{18}H_{25}NO.HBr.H_2O$	*d*-3-methoxy-N-methylmorphinan hydrobromide monohydrate, 37.
$C_{18}H_{25}NO.HBr.2H_2O$	*dl*-3-methoxy-N-methylmorphinan hydrobromide dihydrate, 37.
$C_{19}H_{21}NO_3$	thebaine, 42.
$C_{19}H_{21}NO_3.HCl$	N-allylnormorphine hydrochloride, 55.
$C_{19}H_{21}NO_4$	α-monoacetyl morphine, 51.
$C_{19}H_{23}NO_3.H_2O$	ethylmorphine monohydrate, 49.
$C_{19}H_{23}NO_3.HCl.2H_2O$	ethylmorphine hydrochloride dihydrate, 49.
$C_{19}H_{23}NO_4.HCl.2H_2O$	sinomenine hydrochloride dihydrate, 38.
$C_{20}H_{19}NO_5$	protopine, 32.
$C_{20}H_{21}NO_4$	6,7-dimethoxy-1-veratryl isoquinoline, 28.
$C_{20}H_{21}NO_4.HCl$	6,7-dimethoxy-1-veratryl isoquinoline hydrochloride, 28.
$C_{20}H_{23}NO_4.HCl$	dihydrocodeinone enol acetate hydrochloride, 53.
$C_{20}H_{23}NO_4$	*dl*-laudanine, 30.
$C_{21}H_{23}NO_5$	cryptopine, 31.
$C_{21}H_{23}NO_5$	diacetylmorphine, 52.
$C_{21}H_{23}NO_5.HCl.H_2O$	diacetylmorphine hydrochloride monohydrate, 52.
$C_{21}H_{27}NO$	*dl*-6-dimethylamino-4,4-diphenyl-3-heptanone, 18.
$C_{21}H_{27}NO$	*d*-6-dimethylamino-4,4-diphenyl-3-heptanone, 18.
$C_{21}H_{27}NO$	*l*-6-dimethylamino-4,4-diphenyl-3-heptanone, 18.
$C_{21}H_{27}NO$	*dl*-6-dimethylamino-4,4-diphenyl-5-methyl-3-hexanone, 16.
$C_{21}H_{27}NO.HCl$	*dl*-6-dimethylamino-4,4-diphenyl-3-heptanone hydrochloride, 18.
$C_{21}H_{27}NO.HCl$	*d*-6-dimethylamino-4,4-diphenyl-3-heptanone hydrochloride, 18.
$C_{21}H_{27}NO.HCl$	*l*-6-dimethylamino-4,4-diphenyl-3-heptanone hydrochloride, 18.
$C_{21}H_{27}NO.HCl.H_2O$	*dl*-6-dimethylamino-4,4-diphenyl-5-methyl-3-hexanone hydrochloride monohydrate, 16.
$C_{22}H_{23}NO_7$	narcotine, 27.
$C_{22}H_{23}NO_7.HCl.1/2H_2O$	narcotine hydrochloride hemihydrate, 27.
$C_{22}H_{25}NO_4.1.1/2H_3PO_4.1/2H_2O$	6,7-dimethoxy-1-(4′-ethoxy-3′-methoxybenzyl)-3-methylisoquinoline phosphate hemihydrate, 29.
$C_{22}H_{32}O_3$	1-hydroxy-3-n-hexyl-6,6,9-trimethyl-7,8,9,10-tetrahydro-6-dibenzopyran, 2.
$C_{23}H_{27}NO_8.2H_2O(?)$	narceine dihydrate (?), 23.
$C_{23}H_{27}NO_8.HCl$	narceine hydrochloride, 23.
$C_{23}H_{29}NO_2$	*dl*-6-(N-morpholino)-4,4-diphenyl-3-heptanone, 19.
$C_{23}H_{29}NO_2.HCl$	*dl*-6-(N-morpholino)-4,4-diphenyl-3-heptanone hydrochloride, 19.
$C_{23}H_{31}NO_2.HCl$	*dl*-α-6-dimethylamino-4,4-diphenyl-3-heptanyl acetate hydrochloride, 20.
$C_{23}H_{31}NO_2HCl.1/2H_2O(?)$	*d*-α-6-dimethylamino-4,4-diphenyl-3-heptanyl acetate hydrochloride hemihydrate (?), 20.
$C_{23}H_{31}NO_2HCl.1/2H_2O(?)$	*l*-α-6-dimethylamino-4,4-diphenyl-3-heptanyl acetate hydrochloride hemihydrate (?), 20.
$C_{24}H_{25}NO_3$	benzylmorphine, 50.
$C_{24}H_{25}NO_3.HCl$	benzylmorphine hydrochloride, 50.
$C_{24}H_{31}NO$	*dl*-6-piperidino-4,4-diphenyl-5-methyl-3-hexanone, 17.
$C_{24}H_{31}NO.HCl$	*dl*-6-piperidino-4,4-diphenyl-5-methyl-3-hexanone hydrochloride, 17.
$C_{25}H_{31}NO_3.HCl$	ethylnarceine hydrochloride, 24.
$C_{34}H_{36}N_2O_6.3H_2O(?)$	pseudomorphine trihydrate (?), 56.

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The Ninth Session of the Commission on Narcotic Drugs and the Eighteenth Session of the Economic and Social Council

The Commission on Narcotic Drugs, which held its ninth session in New York from April 19 to May 14, devoted considerable attention to measures of international and national control in the field of narcotic drugs and to implementation of international narcotic treaties. It has not yet finalized the draft code and commentary to the 1953 Opium Protocol and the draft Single Convention which has been under discussion for several sessions. It has, however, taken useful decisions which hold out promising prospects.

The Commission devoted much of its time to scientific subjects, culminating in its decision on synthetic drugs, cannabis, the origin of opium and acetic anhydride. It also considered medico-social questions and the sociological problems to which addiction to narcotic drugs gives rise. It touched upon the field of therapeutics by recommending that governments should prohibit the manufacture, export and import of heroin and ketobemidone and discontinue the medical use of cannabis preparations. Moreover, the Commission was, for the first time, able to agree that the chewing of coca leaf constitutes a form of addiction.

Observers from Argentina, Bolivia, Burma, Colombia, the Federal Republic of Germany, Italy, Japan, Laos, Lebanon, Pakistan, Switzerland, Thailand, the Union of South Africa and Viet-Nam attended the session. The Permanent Central Opium Board, the Drug Supervisory Body, the World Health Organization and the International Criminal Police Commission sent representatives who took part in the discussions. Moreover, a series of Non-Governmental Organizations were represented, namely: the International Confederation of Free Trade Unions, the World Federation of Trade Unions, the International Conference of Catholic Charities, Pax Romana, the International Federation of Women Lawyers, the World's Alliance of Young Men's Christian Associations and the World Union for Progressive Judaism.

The Commission elected as officers: Charles Vaille (France), Chairman; Harry J. Anslinger (United States of America), Vice-Chairman; E. S. Krishnamoorthy (India), Rapporteur.

The Economic and Social Council at its eighteenth session, held in Geneva from June to August 1954, considered the work of the Commission on Narcotic Drugs during its eighth session and approved without practically any change the Commission's proposals.

Reports

The Commission considers it of the utmost importance that governments strictly observe the provisions of the existing international treaties on narcotics and their implementation on the national level by necessary legislative and administrative measures. For this reason, it spent a considerable part of the session studying the annual reports furnished by governments on the working of the international narcotic treaties in their territories as well as the laws and regulations promulgated to give them effect and the reports of important cases of illicit traffic reported to the United Nations.

The Commission was informed by the Secretariat that eighty-four countries participate at present in the international control of narcotic drugs. It was also informed that the flow of annual reports and laws and regulations communicated to the Secretary-General was satisfactory.

The Commission took certain measures to adjust to the present conditions the form of annual reports which governments have to use as guidance when sending their reports to the Secretary-General.

On the Commission's recommendation, the Economic and Social Council called upon governments to ensure close adherence and strict compliance with the provisions of the Conventions of 1925 and 1931 relating to the control of production, manufacture, trade and dis-

tribution, and in particular to carry out promptly and fully their obligations as regards the furnishing of reports, statistics, estimates and other data to the Commission on Narcotic Drugs, the Permanent Central Opium Board and the Drug Supervisory Body.

The Permanent Central Opium Board and the Drug Supervisory Body

With regard to the report of the Permanent Central Opium Board for 1953, the Council took note with satisfaction of this report and recommended, as asked by the Commission, that governments of opium-producing countries indicate how they calculate the amount of their production, exports and stocks as regards the establishment of morphine content and, if possible, water content.

As for the *Estimated World Requirements of Narcotic Drugs in 1954* published by the Drug Supervisory Body, the Commission was impressed by the substantial overestimates made by governments of their needs in narcotic drugs. Thus, in 1952 these overestimates for the world amounted to twenty-five per cent for morphine, twenty-seven per cent for codeine, fifty-four per cent for cocaine and forty-nine per cent for pethidine. The Commission proposed and the Council recommended that governments make sufficient but not excessive estimates, and to accompany them by explanations of the methods employed to calculate the quantities involved.

The Commission and the Council noted with appreciation the work undertaken by the World Health Organization in selecting international non-proprietary names for narcotic drugs as well as for other drugs. They also expressed the view that, for the purpose of ensuring effective narcotics control, it was highly desirable that the existing complicated and slow procedure for the establishment of such names for newly developed narcotics should be simplified and speeded up as much as possible.

Illicit traffic

A new procedure for studying illicit traffic was tried by appointing a Committee on Seizure, consisting of the representatives of Canada, Egypt, Greece, India, Turkey, the United Kingdom and the United States. The Committee was entrusted with the task of making a preliminary report on the documents on illicit traffic which the Commission had before it and of formulating recommendations as to how best the Commission could handle this subject.

As far as illicit traffic in heroin is concerned, the Commission concentrated its attention on the situation in Italy and the Far East. The Italian observer at the Commission explained the measures taken in his country to prevent in the future illicit traffic; in this connexion, the Italian Senate had approved a bill which was before the Chamber of Deputies providing for very severe penalties for illicit manufacture of, and traffickers in, narcotic drugs.

The United States representative pointed out that the heroin seized in many of the cases reported by governments could be traced to the Far East and that most of the heroin entering the western United States came from the Chinese mainland. This statement was strongly opposed by the USSR and Polish representatives. During the discussions on illicit traffic, the Commission had the benefit of the co-operation of the observers of the International Criminal Police Commission.

The Commission on Narcotic Drugs noted that there was a high level of illicit traffic in narcotic drugs which seemed to be increasing. The Economic and Social Council invited, therefore, as proposed by the Commission, governments to co-ordinate their efforts in this sphere, and in doing so to use all existing means and to draw their attention in this connexion to the work of the International Criminal Police Commission.

The Commission was concerned by the possibilities of a growing illicit market in synthetic narcotic drugs. In this connexion it noted that, although they were introduced only in the recent past, there was already evidence of abuse of synthetic drugs and indication of an illicit traffic which may increase to serious proportions. It also pointed out the difficulty of controlling the raw materials used in the manufacture of synthetic narcotic drugs. The Commission decided to reconsider the problem at its next session in the light of the progress made in the studies at present being pursued by the Secretariats of the World Health Organization and of the United Nations in this field.

Making of heroin

The Commission, like its predecessor the League of Nations Advisory Committee on Traffic in Opium and other dangerous drugs, has been aware of the danger of diversion of acetic anhydride for the illicit manufacture of diacetylmorphine (heroin). After discussing the question in closed session, the Commission concluded that, since this substance is widely employed in many countries in a number of industrial operations, it would not be feasible for such countries to subject acetic anhydride to the type of control measures which are applied to narcotic drugs. It did, however, draw the attention of governments to the danger of diversion of acetic anhydride for illicit purposes and suggested that they bear in mind the possibility of action by way of control or surveillance appropriate to the risks involved and the particular circumstances in their countries.

Scientific research

It has been stressed many times that the setting up of an internationally recognized method to establish the origin of opium was of the greatest importance in combating illicit traffic. For several years, United Nations chemists, in co-operation with scientists in several countries, have been conducting experiments in this field. The Commission reviewed the whole subject, basing this review to a considerable extent on the report of a Committee of Chemical Experts appointed by the Secretary-General in accordance with a previous Economic and

Social Council resolution. In performing this task, the Commission was fortunate in hearing the comments of several participants in the research program, Dr. Liang, Dr. Panopoulos and Dr. Farmilo, members of the Chinese, Greek and Canadian delegations to the Commission respectively.

The Commission recommended and the Council adopted a resolution (i) reaffirming the importance that is attached to the programme of opium research; (ii) expressing its satisfaction with the work done thus far; (iii) calling for further research; (iv) requesting governments to furnish samples of opium licitly and illicitly cultivated within their countries, as well as important samples of opium seizures from the international illicit traffic; (v) instructing the Secretary-General to request these samples from governments and further to develop the Secretariat's opium research deferring all other laboratory work except that connected with determining origin.

Both the Commission and the Council considered that it would be very useful to set up a United Nations narcotics laboratory and the Council referred to the General Assembly, for consideration in connexion with its review of the Secretary-General's reorganization of the United Nations Secretariat proposals, the question of the establishment of such a narcotics laboratory. The Council requested the Secretary-General to provide the General Assembly with all information relating to the establishment of the laboratory, including comparative costs and advantages of locating it in New York or Geneva.

The Opium Protocol of 1953

The Council at its sixteenth session had requested the Commission to draw up a model code and commentary for the application of the Protocol. The Commission chose Charles Vaille, representative of France, as rapporteur to prepare a draft for consideration at the Commission's tenth session. This he will do after consultation with the Permanent Central Opium Board, the Drug Supervisory Body and the Secretariat.

Article 6 of the 1953 Protocol provided that the Parties shall not permit the import and export of opium other than opium produced in seven countries listed in the Protocol. But no provision in the Protocol prevents a country from producing opium for its own consumption. Some members of the Commission expressed concern about reports that production was being contemplated in certain countries other than the seven listed in the protocol authorizing the cultivation of opium. The Commission expressed the fear that, if production of opium was now begun in countries which had not in recent years engaged in such production, the existing over-production would be seriously aggravated.

As requested by the Commission, the Council urged the governments of all countries in which there has been no production of opium in recent years to prohibit such production in the future.

Draft Single Convention

The Commission continued the discussion of the draft Single Convention and considered sections dealing with internal trade, possession of drugs, measures of supervision, penal provisions, cure of the drug habit and some sections relating to general provisions. With respect to penal provisions, the Commission adopted, with a few amendments, a United Kingdom proposal. Experience has shown in the field of narcotic drugs as well as in other fields of co-operation against international crime that there are great difficulties in establishing universally applicable rules of penal law. Only nineteen States became parties to the 1936 Convention which requires States to apply certain rules of penal law intended to ensure prosecution and punishment of offenses committed abroad, as compared with forty-three parties to the 1948 Protocol or seventy States which became parties to the 1931 Convention. The Commission hoped that the text it had adopted would be more generally acceptable than the 1936 Convention. The Council called upon the Commission to give priority at its next session to the elaboration of the Single Convention.

Drug addiction

In a general discussion on drug addiction, the Commission agreed on the importance of maintaining this topic on its agenda and of discussing it at the international as well as national levels. It was pointed out that drug addiction must also be approached from a subjective or "cause and treatment" point of view in addition to the historic "preventive or control" approach. Many delegations were agreed that the most important part of treatment was that which followed clinical withdrawal of the drug, i.e., the psychotherapeutic and rehabilitative stages.

Some representatives stated that in their view unsatisfactory social conditions were mainly responsible for the social evil of addiction and that, by remedying such conditions in their own countries, addiction had almost totally disappeared. Other members of the Commission felt, however, that not enough was known of the causes and extent of drug addiction in the world today and that further surveys were needed. They also thought that the knowledge made available to the United Nations would have an enhanced value if it could be presented on a comparable basis. The Commission believed that, in view of its present knowledge, studies must be made along empirical lines.

The Council decided, as recommended by the Commission, to call the attention of the governments concerned to the necessity of having, as soon as possible, in accordance with domestic law and public policy, systematic arrangements for the effective control and the registration of addicts by health authorities. It stressed the importance of governments considering the setting up of means for the treatment, care and rehabilitation of drug addicts, on a planned and compulsory basis, in properly conducted institutions. It also requested the Secretary-General to continue his studies and to express

appreciation to the World Health Organization for the work carried out by this Organization in this field.

Diacetylmorphine

The Commission considered the problem of diacetylmorphine (heroin) in the light of a resolution by the Sixth World Health Assembly recommending prohibition of the manufacture and importation of that substance. It noted that, according to a survey made by WHO, fifty-six States had declared themselves in favor of dispensability of diacetylmorphine while only seven States had expressed opposite views.

Most members were in agreement that some form of international action aimed at prohibiting this dangerous drug should be taken.

As to the type of action which should be taken, the Commission decided not to recommend the conclusion of an interim agreement, but to include suitable provisions in the proposed Single Convention. In the meantime, the Council urged all governments to prohibit the manufacture, import and export of diacetylmorphine and its salts, preparations, and preparations of its salts, except for such small amounts as may be necessary for scientific purposes only.

Synthetic drugs

The Commission held a general debate on the various problems arising out of the continual introduction into the field of medicine of new synthetic narcotic drugs. It noted with satisfaction that as of January 1, 1954, forty-three States had become parties to the Protocol signed at Paris on November 19, 1948, bringing under international control drugs outside the scope of the Convention of July 13, 1931, for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs. This Protocol is specially aimed to bring under international control the ever increasing number of new synthetic narcotic drugs.

Upon the Commission's recommendation, the Council adopted a resolution which: (i) called upon all States not parties to the 1948 Protocol to become parties in accordance with article 5 of that Protocol; (ii) called the attention of all governments to the necessity for strict control over the possession, manufacture, import and export of, trade in, and use of synthetic narcotics; (iii) invited all governments to consider the possibility of carrying out a systematic campaign among members of the medical profession to alert them to the danger of addiction inherent in the use of synthetic narcotics and to the necessity of exercising great care in prescribing such drugs; (iv) recommended that all governments submit provisionally, pending a decision by WHO, each drug notified to the Secretary-General under Article 1 of the 1948 Protocol to the narcotics régime and, in particular, to the import and export controls provided for by chapter V of the 1925 Convention; and (v) invited governments to study the desirability of exercising the requisite supervision over certain intermediary products, used in the manufacture of synthetic narcotics or of prohibiting their manufacture.

There was no agreement in the Commission on the question whether synthetic drugs should be totally prohibited or their number limited except, of course, in regard to those drugs which had particularly powerful addiction-producing properties and no distinct therapeutic advantages over other less dangerous drugs. These, it was agreed, should be banned. In pursuance of this idea, the Economic and Social Council urged governments to prohibit the manufacture, import and export of ketobemidone, its salts, preparations and preparations of its salts. Ketobemidone, it was agreed, was a very dangerous addiction-producing synthetic drug.

Cannabis

The Commission noted the opinion expressed by the Expert Committee on drugs liable to produce addiction of the World Health Organization that "there is no justification for the medical use of cannabis preparations" and that these preparations "are practically obsolete". The Economic and Social Council, as asked by the Commission, recommended that governments of countries in which such preparations were still being used for medical purposes explore the possibility of discontinuing their use, with a view to discontinuing such use as rapidly as possible.

The Commission approved a series of comparative studies on the cannabis situation in different regions of the world. The representative of WHO stated that his organization hoped to finish a study on the physical and mental effects of the use of cannabis in time for the Commission's session in 1955.

The Commission expressed concern about the steadily increasing illicit traffic in the parts of the plant *Cannabis sativa L* containing resin, in many different regions of the world. The plant *Cannabis sativa* is, however, widely cultivated in many parts of the world for industrial purposes, i.e., for production of fibre and seed, and the Commission had apprehension that there was a danger of such industrial cultivation becoming in some countries a source of illicit traffic. The Council, therefore, as requested by the Commission, invited the governments concerned to furnish such information to the Secretariat of the Food and Agriculture Organization as may be required to carry out a study on the possibility of replacing *Cannabis sativa L* by a variety of the same plant or by other plants serving similar industrial purposes, but not containing harmful resin, and to FAO in consultation with the United Nations Secretariat, to prepare this study.

Coca-leaf problem

In the view of the Commission, decisive progress was made during its ninth session in connexion with this question. For the first time the representatives of all the countries mainly concerned—all of which took part in the Commission's consideration of the matter either as members (Peru) or as observers (Argentina, Bolivia

and Colombia)—agreed that the habit of coca-leaf chewing constitutes a form drug addiction and his harmful. The Commission itself unanimously considered that coca-leaf chewing was a drug addiction. It shared the view of these representatives that many difficulties were inherent in the abolition of the chewing, to which large numbers of the aboriginal population were addicted, and that a cautious and gradual approach was required to find a solution of the problem. The Peruvian representative made a detailed statement on the problem of the coca-leaf chewing and in particular the measures that the Government of Peru had taken already to solve it—not only administrative measures but also intensive health and educational programmes. He noted that quick results could not be expected and that it would be necessary to request technical assistance from the United Nations and the specialized agencies. The Commission welcomed his statement. As proposed by the Commission, the Council expressed its satisfaction at the policy adopted by the governments concerned, and particularly by that of Peru, regarding the progressive abolition of this habit.

It further recommended that the technical assistance services of the United Nations and the specialized agencies give due consideration to any requests which the countries concerned may make for assistance in developing appropriate administrative or social measures for the gradual suppression of the habit or other remedial measures including requests for various experiments which might be necessary.

The Council finally recommended that the governments concerned: (i) limit gradually and as quickly as practicable the cultivation and the export of coca leaf to medical, scientific and other legitimate purposes; (ii) continue their efforts to abolish progressively the habit of coca-leaf chewing in their respective countries; (iii) limit progressively the importation of coca leaf for the purpose of chewing; and (iv) continue their programmes of health education, and in any case where such programmes do not yet exist, to initiate them, for the purpose of making known to the populations affected by the habit the dangers of said habit, of preventing its extension and of facilitating the efficacy of the measures adopted or about to be adopted.

Sir Thomas Wentworth Russell

On April 10th 1954 Sir Thomas Wentworth Russell, K.B.E., C.M.G., widely known throughout the world as Russell Pasha, died in London.

For everybody connected with the control of narcotics, Russell Pasha was not only a legendary figure but a man well known from the days of the Advisory Committee of the League of Nations where, ever since his first appearance in January 1930, he impressed all those who had the honour and the pleasure of working with him with his great intelligence, his profound knowledge of everything connected with narcotics and his keen sense of humour which showed a deep understanding of human nature.

Born on 22 November 1879, educated at Haileybury and Trinity College, Cambridge, he joined the Egyptian Civil Service in 1902 and formed the Camel Corps before becoming, in 1917, commandant of the Cairo Police, a post in which he showed himself both efficient and resourceful. As head of the Central Narcotics Intelligence Bureau, which the Egyptian Government set up in 1929, he was responsible for the outstanding reports to the Advisory Committee which still constitute a very important source of information on illicit traffic and illicit traffickers. He was not only a great civil servant but a man of action and some of the episodes he described in his fascinating book *Egyptian Service* are more exciting than any fiction.

With him disappeared a great international figure. The *Bulletin on Narcotics* wishes to extend its heartful condolence to his family.

Bibliography

SYNTHETIC DRUGS

Part III. METHADONE AND RELATED COMPOUNDS

Part IV. MORPHINAN AND MORPHINE SYNTHESIS

Part V. DITHIENYLBUTENYLAMINES

Part III

METHADONE AND RELATED COMPOUNDS

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Part IV

MORPHINAN AND MORPHINE SYNTHESIS

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Part V

DITHIENYLBUTENYLAMINES

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